

Experience from a prevention trial within a cohort of youth at high risk of severe mental illness

Rudolf Uher

Dalhousie University, Nova Scotia, uher@dal.ca ; www.forbow.org

TwICs, London

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Conflicts of interest & funding

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Consulting	World Health Organization
Advisory	none
Shares	none

Aim: Prevent Severe Mental Illness

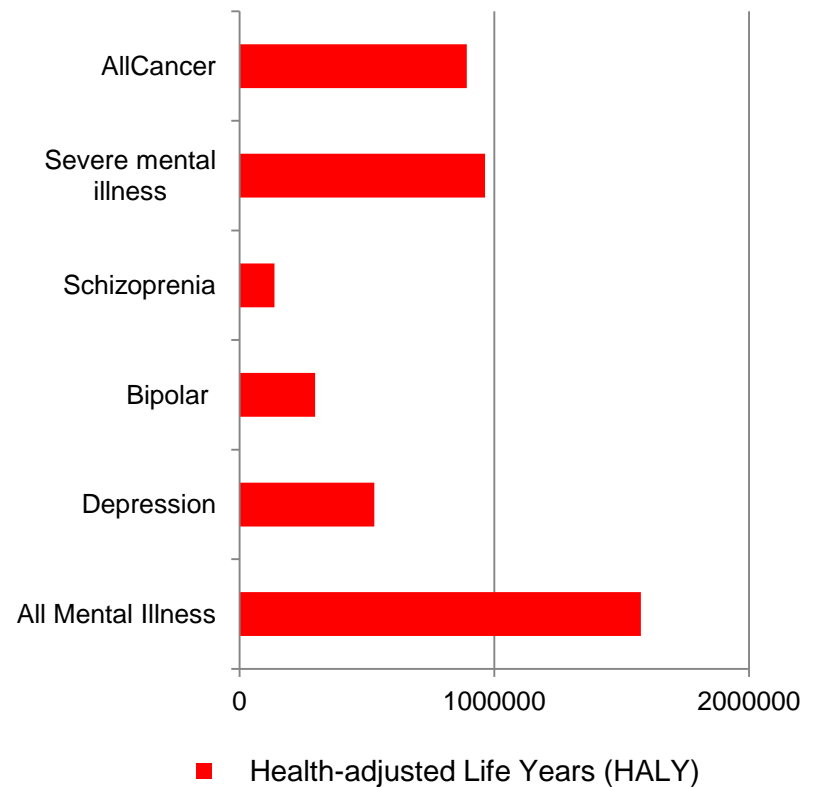
Diagnoses

- Schizophrenia
- Bipolar disorder
- Major depressive disorder

Severity criteria

- Recurrent
- Chronic
- Requires hospital admissions
- Psychotic symptoms
- Life-threatening suicide attempt

Burden of Illness



Severe Mental Illness

- Runs in families: risk increased 4-8 times in offspring of affected parents
- Onset early in life, typically between age 15 and 25 years
- Preceded my milder psychopathology in childhood (antecedents)

Indicated prevention

1. Identify individuals at risk
2. Intervene

Risk Identification Strategy

GENETIC RISK

- Family history
- Polygenic risk

ANTECEDENTS

1. Affective lability
2. Anxiety
3. Psychotic symptoms
4. Basic symptoms

The Problem

We can predict risk early, but most children at risk are not seeking help.

Acceptability Challenge

Call to a non-treatment seeking participant:

“We would like to offer you / your daughter / your son an intervention to reduce the risk of mental illness.”

STUDY PROTOCOL

Open Access

Preventing mood and anxiety disorders in youth: a multi-centre RCT in the high risk offspring of depressed and anxious patients

Maaïke H Nauta^{1*}, Helma Festen¹, Catrien G Reichart², Willem A Nolen³, A Dennis Stant⁴, Claudi L H Bockting¹, Nic J A van der Wee⁵, Aartjan Beekman⁶, Theo A H Doreleijers⁷, Catharina A Hartman³, Peter J de Jong¹ and Sybolt O de Vries^{3,8}

Abstract

Background: Anxiety and mood disorders are highly prevalent and pose a huge burden on patients. Their offspring is at increased risk of developing these disorders as well, indicating a clear need for prevention of psychopathology in this group. Given high comorbidity and non-specificity of intergenerational transmission of disorders, prevention programs should target both anxiety and depression. Further, while the indication for preventive interventions is often elevated symptoms, offspring with other high risk profiles may also benefit from resilience-based prevention programs.

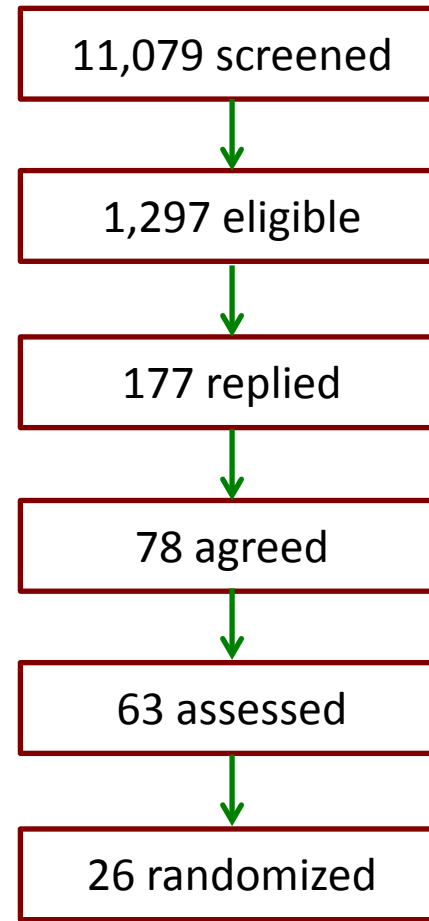
Method/design: The current STERK-study (Screening and Training: Enhancing Resilience in Kids) is a randomized controlled clinical trial combining selected and indicated prevention: it is targeted at both high risk individuals without symptoms and at those with subsyndromal symptoms. Individuals without symptoms meet two of three criteria of the High Risk Index (HRI; female gender, both parents affected, history of a parental suicide (attempt)). This index was developed in an earlier study and corresponds with elevated risk in offspring of depressed patients. Children aged 8–17 years ($n=204$) with subthreshold symptoms or meeting the criteria on the HRI are randomised to one of two treatment conditions, namely (a) 10 weekly individual child CBT sessions and 2 parent sessions or (b) minimal information. Assessments are held at pre-test, post-test and at 12 and 24 months follow-up. Primary outcome is the time to onset of a mood or anxiety disorder in the offspring. Secondary outcome measures include number of days with depression or anxiety, child and parent symptom levels, quality of life, and cost-effectiveness. Based on models of aetiology of mood and anxiety disorders as well as mechanisms of change during

Acceptability of Intervention in Non-treatment Seeking High-Risk youth

RCT

- Offspring of parents with depression or anxiety
- Age 8-17
- CBT (10 child + 2 parent sessions)

*Trial terminated after 30 months
due to lack of enrolment.*



RESEARCH ARTICLE

Open Access

Parents' perceptions on offspring risk and prevention of anxiety and depression: a qualitative study

Helma Festen^{1*}, Karen Schipper², Sybolt O de Vries³, Catrien G Reichart⁴, Tineke A Abma^{2,5} and Maaïke H Nauta^{1,6}

Abstract

Background: Offspring of patients with anxiety or depression are at high risk for developing anxiety or depression. Despite the positive findings regarding effectiveness of prevention programs, recruitment for prevention activities and trials is notoriously difficult. Our randomized controlled prevention trial was terminated due to lack of patient inclusion. Research on mentally-ill parents' perceptions of offspring's risk and need for preventive intervention may shed light on this issue, and may enhance family participation in prevention activities and trials.

Methods: Qualitative data were collected through semi-structured interviews with 24 parents (patients with anxiety or depression, or their partners). An inductive content analysis of the data was performed. Five research questions were investigated regarding parents' perceptions of anxiety, depression, and offspring risk; anxiety, depression, and parenting; the need for offspring intervention and prevention; and barriers to and experiences with participation in preventive research.

Results: Parental perceptions of the impact of parental anxiety and depression on offspring greatly differed. Parents articulated concerns about children's symptomatology, however, most parents did not perceive a direct link between parent symptoms and offspring quality of life. They experienced an influence of parental symptoms on family quality of life, but chose not to discuss that with their children in order to protect them. Parents were not well aware of the possibilities regarding professional help for offspring and preferred parent-focused rather than offspring-focused interventions such as parent psycho-education. Important barriers to participation in preventive research included parental overburden, shame and stigma, and perceived lack of necessity for intervention.

Conclusions: This study highlights the importance of educating parents in adult health care. Providing psycho-education regarding offspring risk, communication in the family, and parenting in order to increase parental knowledge and parent-child communication, and decrease guilt and shame are important first steps in motivating parents to participate in preventive treatment.



FAMILIES OVERCOMING RISKS AND BUILDING
OPPORTUNITIES FOR WELL-BEING

STUDY DESIGN

Design



- Accelerated cohort
 - offspring age at enrolment 0 - 21 years
 - annual follow-ups (12 ± 1 months)
 - until age 27 years
 - linkage with administrative data
- Embedded randomized trial(s)
 - eligibility based on cohort assessments
 - eligible participants randomly selected to be offered intervention
 - comparator = no intervention offered
 - outcomes derived from cohort follow-ups



THE COHORT

The FORBOW cohort



Offspring

- 306 youth
(154 boys, 152 girls)
mean age 10 years
(SD 4.8, range 1-21 years)
- 700 assessments
(baseline + annual follow-ups)
 - time 1 306
 - time 2 200
 - time 3 149
 - time 4 51

Parents

- 308 parents
(132 fathers, 174 mothers)
 - 26 schizophrenia
 - 74 bipolar
 - 86 depression
 - 24 other diagnosis
 - 98 no diagnosis

enrolment ongoing (target = 600 youth)

Uher R, Cumby J, MacKenzie LE, Morash-Conway J, Glover JM, Aylott A, Propper L, Abidi S, Bagnell A, Pavlova B, Hajek T, Lovas D, Pajer K, Gardner W, Levy A, Alda M. A familial risk enriched cohort as a platform for testing early interventions to prevent severe mental illness. *BMC Psychiatry*. 2014 Dec 2;14:344.

The first 300 offspring

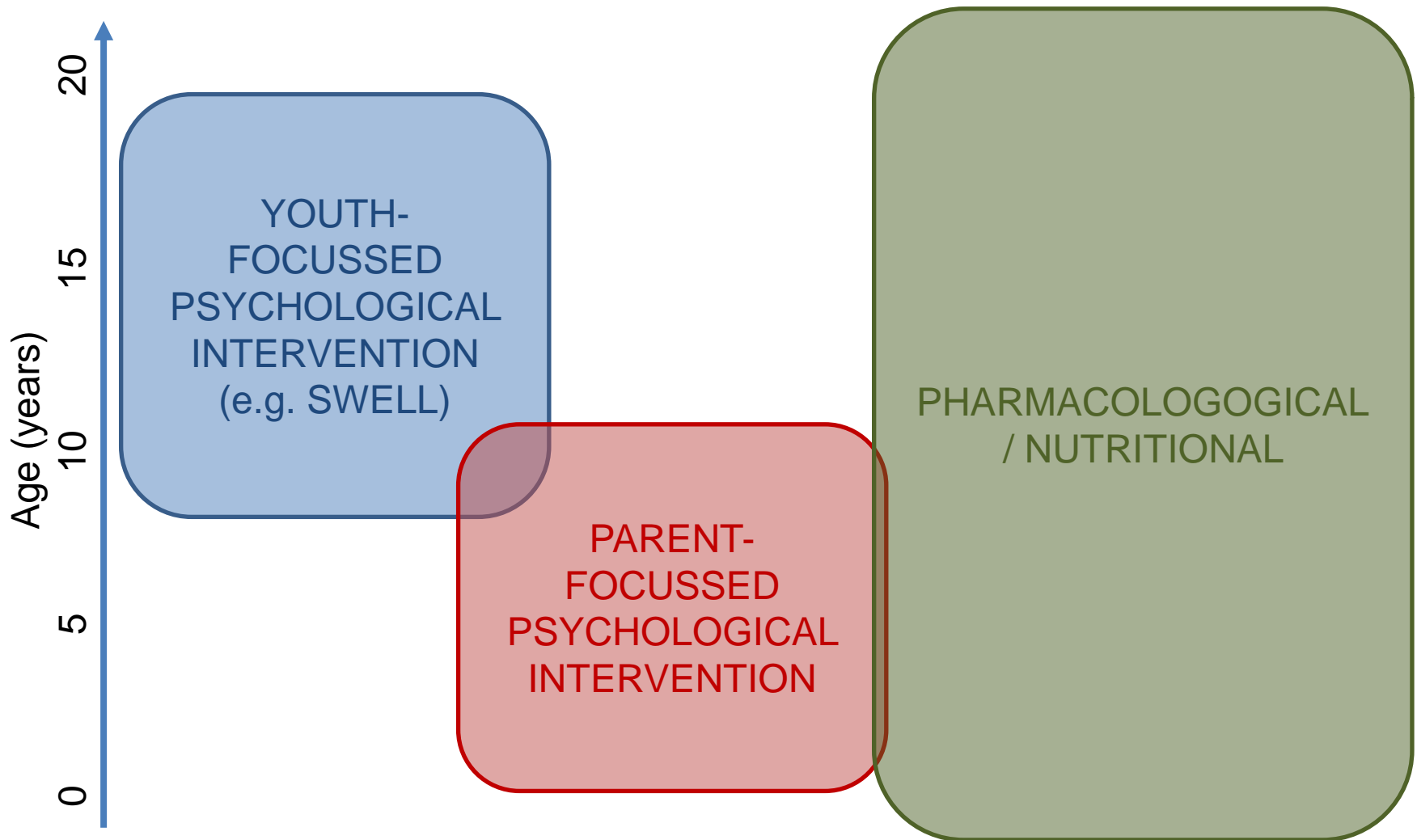


	Offspring	
Parent's diagnosis	No diagnosis	67
	Depression	126
	Bipolar	81
	Schizophrenia	26
		300



THE INTERVENTIONS

Pre-emptive early interventions



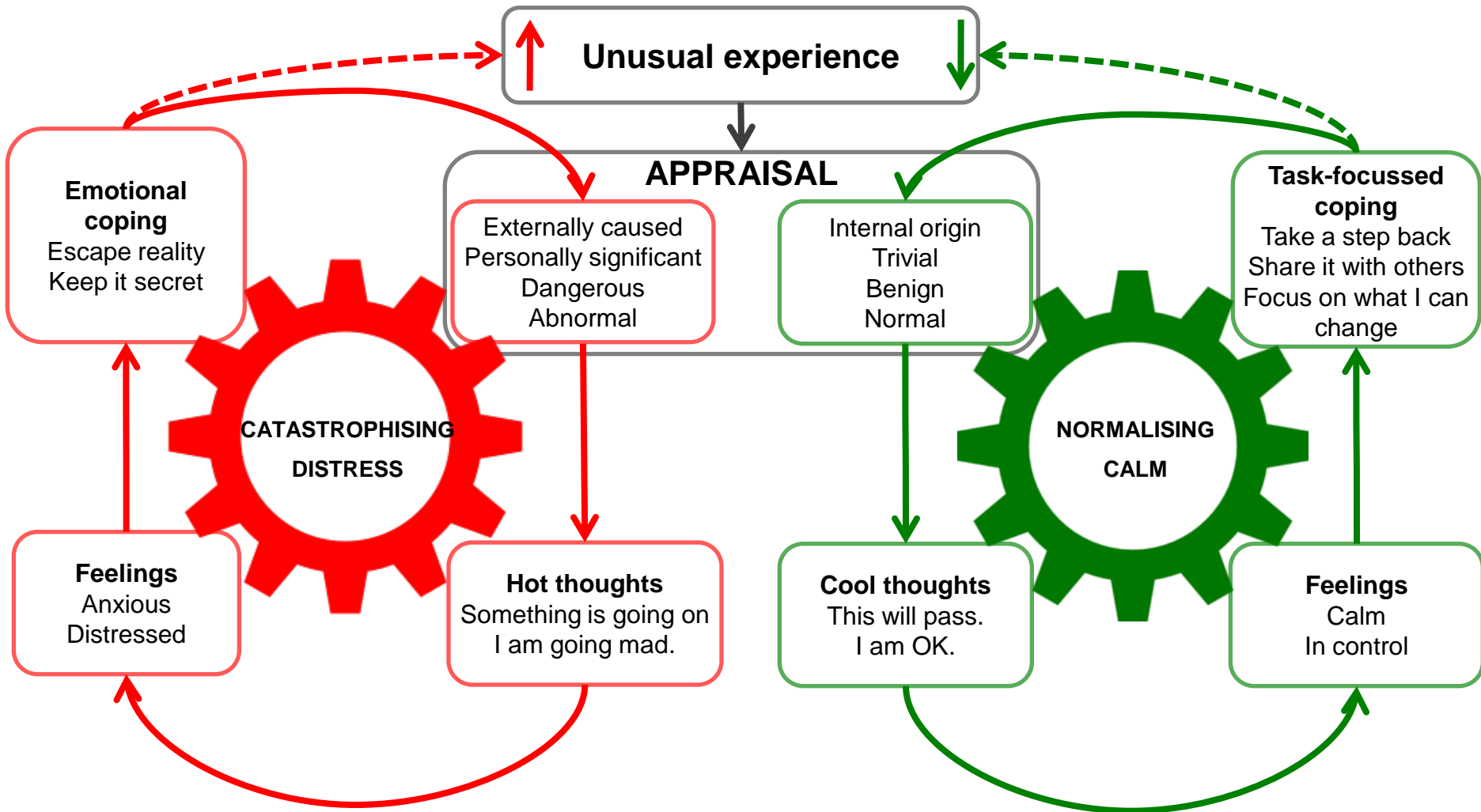
Skills for Wellness

Format:

- youth-focused (age 9-19)
- one-on-one (individual)
- face-to-face
- 8-16 one-hour sessions
- over 3-4 months
- focus on skill-building

Modules – content:

- Core modules
 - Normalization
 - Realistic thinking
 - Present moment focus
 - Problem solving
- Antecedent-modules
 - Affective lability
 - Anxiety
 - Psychotic symptoms
 - Basic symptoms



Skills for Wellness: Eligibility

Inclusion:

- Age 9-21
- One or more antecedents
- Commutable distance (\leq 1 hour)
- Consent to participate in intervention studies

Exclusion:

- Psychological treatment in past 12 months
- Severe mental illness (SMI)
- Autism spectrum disorder
- General intellectual disability

Acceptability Challenge

Call to a non-treatment seeking participant:

“We would like to offer you / your daughter / your son a course of sessions to strengthen your/her/his mental health skills. Would you/she/he be interested? ”



ETHICS

REB approval process

1. FOROW approved as a cohort study with cohort-multiple randomized controlled design and the potential to include one or more intervention trials.

Consent included:

- “... to be approached with offers of courses and programs that we believe may help some people strengthen their health and reduce the risk for mental health problems”
- “...use the information you give us to evaluate how useful these courses or programs might be”

2. SWELL approved separately as the first intervention trial within the FORBOW cohort

REB stage I: FORBOW Cohort

- Cohort study approved in first sitting with minor corrections requested, including:
 - Option to be included or not in intervention studies
 - Option to be included or not in genetic studies
- Most comments concerned participant burden, privacy and risk of stigma
- No concerns were raised about the cmRCT / TwiC design

REB stage II: SWELL Intervention

- Three rounds of full board review and revisions
- Specific issues included:
 - “Controls need to understand their data use and part in this research”
 - “Board believes that this is not fair for the control group who will not have the opportunity to receive intervention”
- PI invited to attend and explain the need for and advantages of the ‘unusual’ design
- On third review, protocol approved without major changes in design

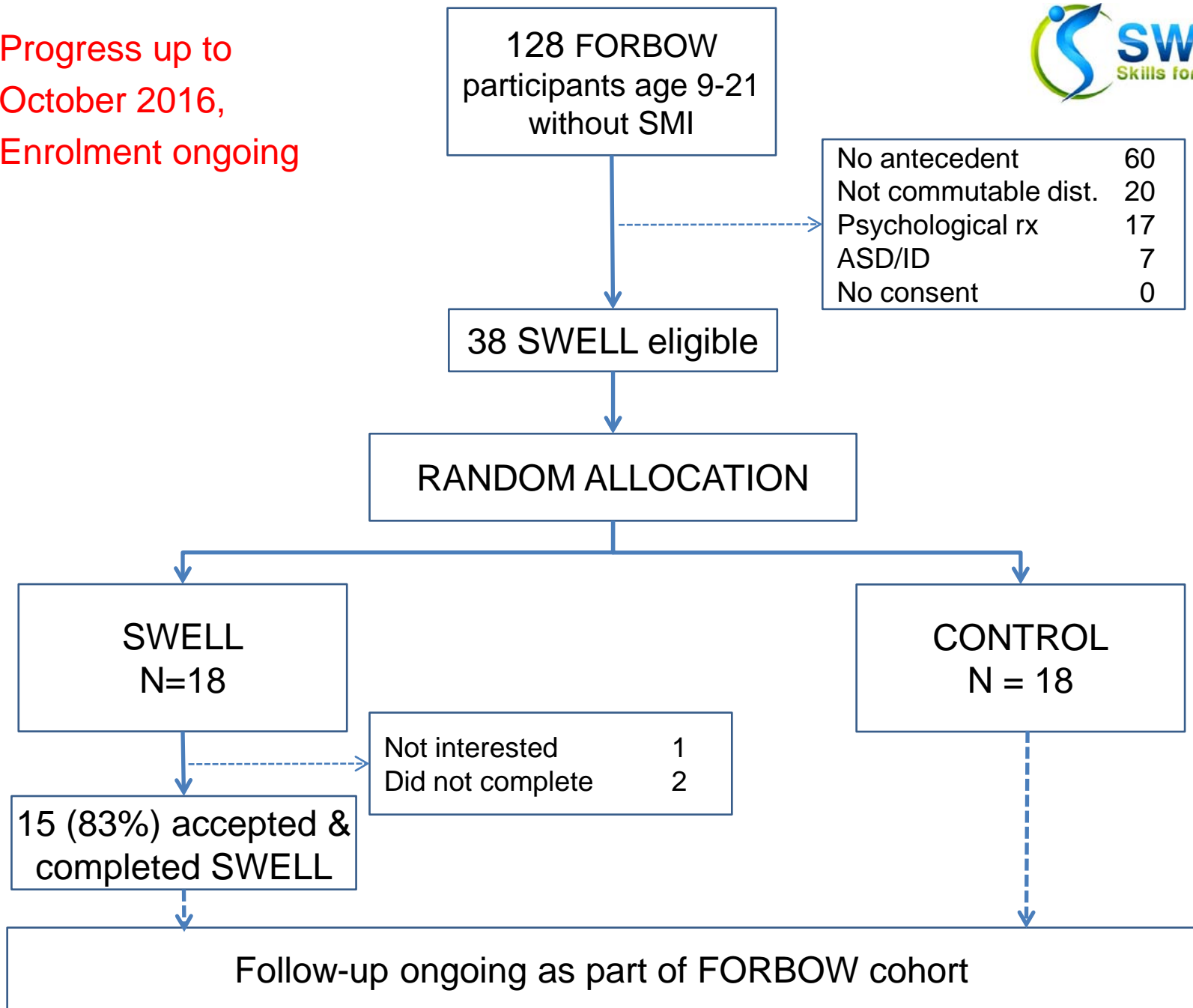


EXPERIENCE TO DATE

Experience to-date

- 306 participants enrolled in cohort
- 95% retention on annual follow-ups
- 38 intervention-eligible participants
- 18 allocated to SWELL intervention
- 15/18 (83%) accepted and completed SWELL
- No adverse event / complained related to intervention allocation

Progress up to
October 2016,
Enrolment ongoing

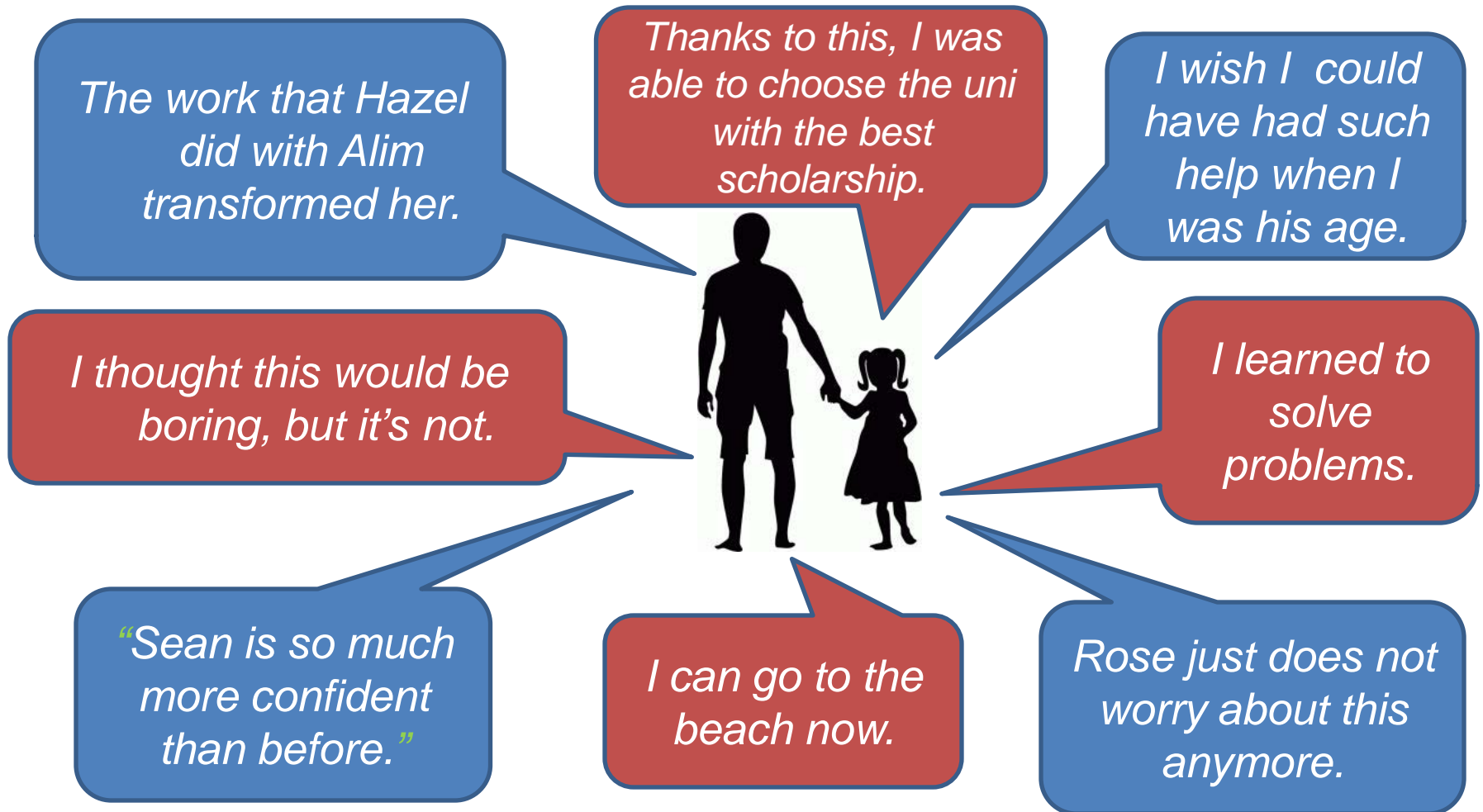


How has your week been?

Tick one box for each question that best describes how you have been over the past 7 days.

	<i>Never</i>	<i>Once or twice</i>	<i>Often</i>	<i>All the time or Every day</i>
I felt nervous around people I don't know well.	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
I felt miserable or unhappy.	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
I lost my temper.	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
I didn't enjoy anything at all.	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
All of a sudden I felt really scared for no reason at all.	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
I suddenly became nervous and fidgety.	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
I worried about the future.	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
I was angry.	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
I felt too tired to do anything.	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
I worried about going to school or work.	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
I had bursts of silliness.	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
I felt I was a bad person.	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
I worried about not being as good as others.	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
I thought nobody really loved me.	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
I got easily annoyed by others.	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
I had difficulty falling asleep.	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
I woke up during the night and could not get back to sleep.	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
I suddenly became sad for no apparent reason.	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
I heard voices or noises that other people could not hear.	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
I saw something or someone that other people could not see.	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
I thought I was being followed or spied on.	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>

What do participants say?



Media coverage and study integrity

- Intervention is an attractive part of our research program
- Tension between need to inform the public and design where participants are enrolled in a cohort (rather than directly into an intervention study)

Conclusions

- Dichotomy between intervention and non-intervention in REB approval process
- Youth-focussed psychological intervention can be made highly acceptable high-risk youth and their families
- Acceptability of SWELL intervention much higher than in a previous study that used traditional RCT design in similar population (83% vs. 2% agreement rate)
- Challenge of participants motivated to enter an intervention study

Directions

- Interventions for children age 3-6
- Use of genetic data to select participants

Thank you!



Investigators

Sabina Abidi
Martin Alda
Alexa Bagnell
Bill Gardner
Tomas Hajek
Adrian Levy
Dave Lovas
Joanne MacDonald
Jason Morrison
Kathleen Pajer
Barbara Pavlova
Lukas Propper
Phil Tibbo

FORBOW team

Alyson Zwicker
Elaine Skene
Emily Bedford
Heather Oland
Heather Reckling
Jackie Glover
Jessica Morash
Jill Cumby
Lynn MacKenzie
Shannon Neville
Victoria Patterson
Vlad Drobinin
Zeina Asyyed

SWELL team

Alim Awadia
Alexa Bagnell
Jason Morrison
Barbara Pavlova
Alissa Pencer

Residents

Alice Aylott
Daniel Rasic

Database

Joe Fraser
Chris Theriault

Advisory

Jean Addington
Louise Arseneault
George W. Brown
Avshalom Caspi
Helen Fisher
Jeff Gagne
Louise M. Howard
Joan Kaufman
Cathryn Lewis
Temi Moffitt
John I. Nurnberger
Michael Rutter
Frauke Schultze-Lutter