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Smile

Sensible Medical Innovations Lung fLuid status monitor allows rEducing readmission rate of heart failure patients

NCT02448342

SMILE Clinical Trial

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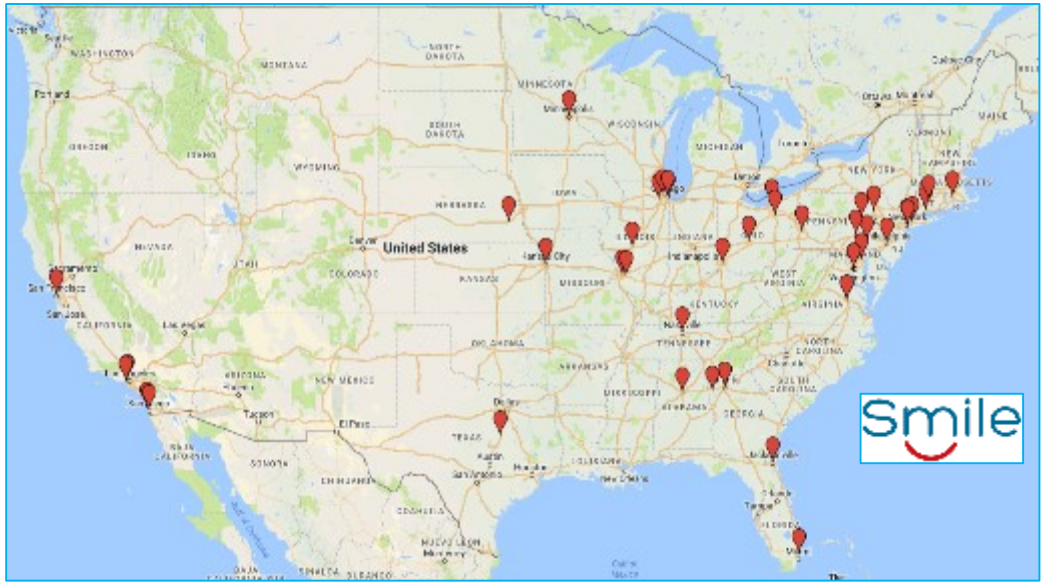
- Post-FDA study for reimbursement and market adoption
- Daily ReDS monitoring to guide treatment for reducing HF readmission rate
- 43 US Sites
- 268 Patients
  - Stopped early - planned for 380
  - 135 ReDS patients
  - 133 SOC patients
- Follow-up – 6.1 ± 3.4 months
- Readmissions were collected and adjudicated by CEC



ReDS-guided Heart Failure Management

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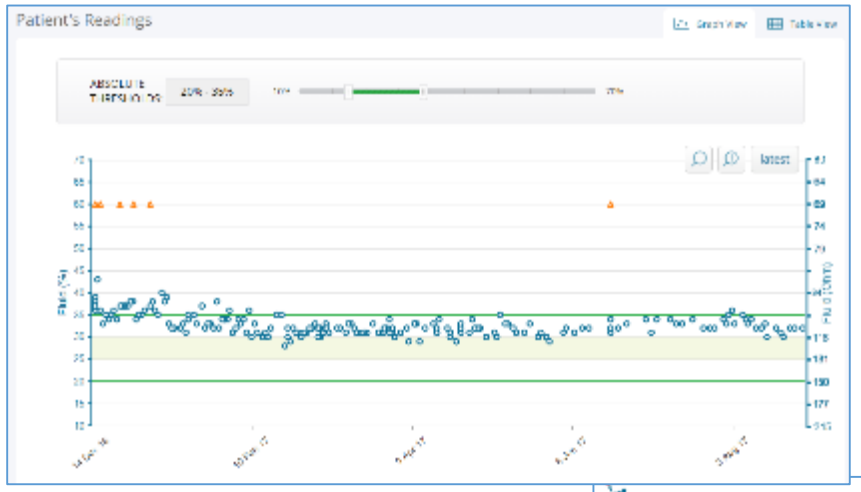
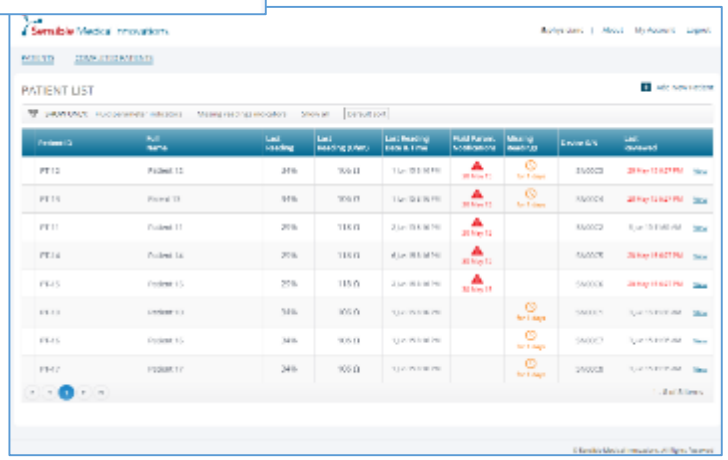
ReDS System

ReDS Cloud





ReDS Treatment Algorithm

- **Focused electromagnetic RADAR beam through the right lung**
- **Absolute measurement of lung fluid content**
- **Normal lung measures 20-35% lung fluid content**
- **90 seconds measurements and no skin contact**

Study Design

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- Prospective, Randomized, Controlled, Multi-center Trial (open label)
- ReDS-guided treatment vs. Standard of Care management
- Methods:
  - All patients:
    - Enrollment during ADHF hospitalization or within 10 days following discharge
  - ReDS patients:
    - Daily ReDS measurements at home – patients blinded to ReDS results
    - Readings sent to physicians using HIPAA-compliant dedicated cloud-based system; clinicians could log in and review readings at anytime
    - Automatic Notifications were sent for out of range readings (default: 20-35%)
    - Patients were to be treated according to a ReDS-guided treatment protocol

Study Flow

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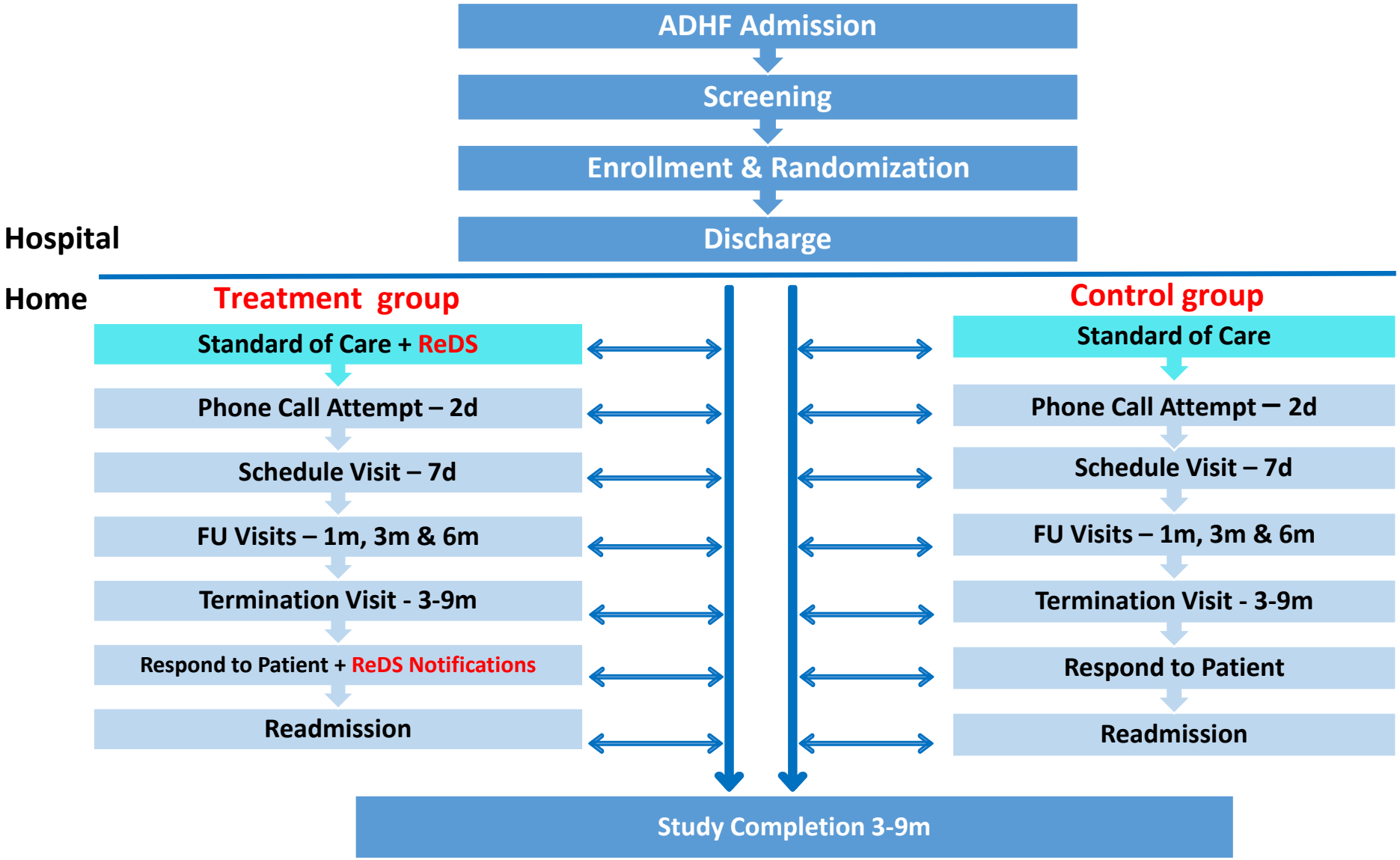

Study Endpoints

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- **Primary Efficacy Endpoint**
  - The rate of recurrent events of HF readmissions during entire follow-up period
- **Secondary Efficacy Endpoints**
  - Time from discharge until the first event of HF readmissions through the entire follow-up period
  - Proportions of total days lost to hospitalization due to HF events
  - Time from discharge until all-cause mortality through entire follow-up period

Statistical Analyses

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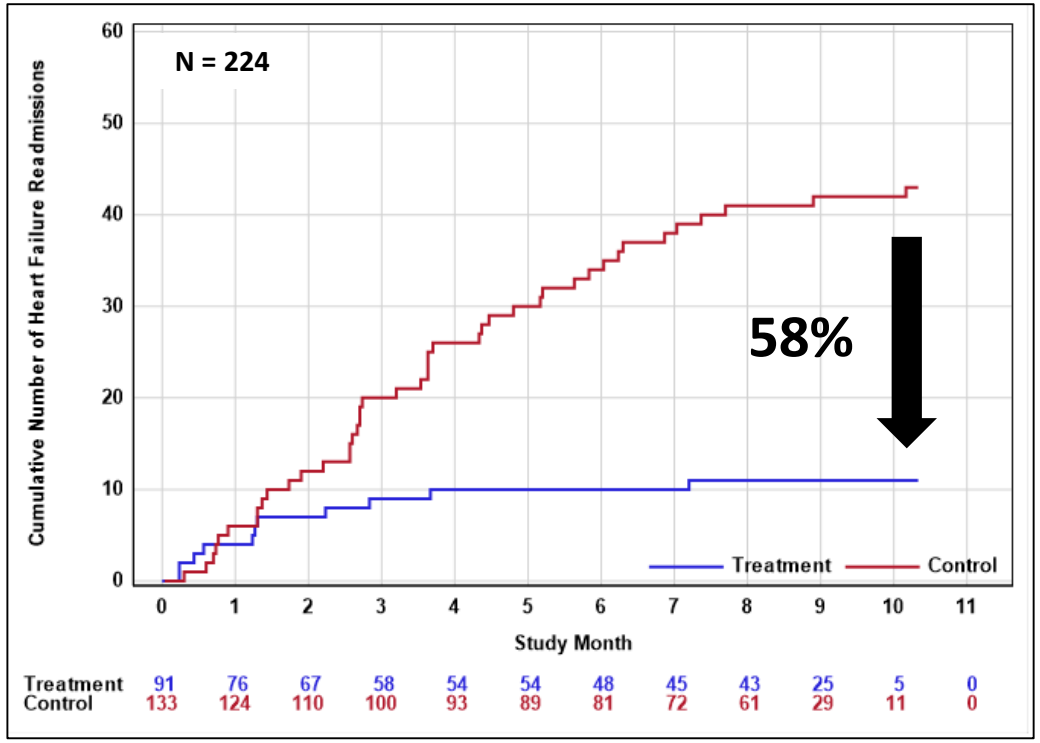
- Primary endpoint analyzed using the method of Anderson and Gill (A-G)
- ReDS-based-treatment (Modified ITT population) defined by
  - No ReDS measurements for > 20 consecutive days, or
  - No ReDS-guided treatment although > 8 threshold notifications sent
- Robustness was confirmed by a Sensitivity and propensity matched analyses
  - Same propensity matching analysis was performed by CHAMPION due to FDA request to account for adherence

Patient Characteristics

Parameter	Treatment (N = 135)	Control (N = 133)
Age (year)	69 (12) [35.1 92.3]	68 (13) [35.0 90.5]
Male sex	95 (70%)	93 (70%)
White	87 (64%)	76 (57%)
BMI (kg/m²)	29 (4) [20.4 37.1]	29 (4)
NYHA I,II, III, IV (%)	(5,25,64,6)	(2,25,63,10)
ACC/AHA Heart Failure Stage C	112 (85%)	112 (84%)
LVEF (≥40%)	41 (31%)	34 (27%)
Time from HF diagnosis (year)	6 (7) [0 47.7]	5 (6) [0 23.3]
Number of Previous HF hospitlazation	3 (3) [0 15]	3 (2) [0 13]
CRT-D	11 (8%)	12 (9%)
CRT-P	1 (1%)	1 (1%)
ICD	35 (26%)	39 (29%)
Pacemaker	9 (7%)	13 (10%)
Comorbidities		
Hypertension	103 (78%)	100 (76%)
Coronary artery disease	64 (49%)	62 (47%)
Diabetes mellitus	71 (54%)	62 (47%)
Atrial fibrillation	65 (49%)	70 (53%)
Chronic obstructive pulmonary disease	27 (20%)	30 (23%)
Laboratory and hemodynamic analyses		
Creatinine (mg/dL)	1.5 (0.5) [0.6 3.0]	1.5 (0.5) [0.5 4.2]
GFR (mL/min per 1·73m²)	62 (26) [21 152]	65 (31) [24 226]
Systolic blood pressure (mm Hg)	121 (20) [83 183]	118 (19) [81 173]
Diastolic blood pressure (mm Hg)	68 (13) [37 104]	70 (12) [44 95]
Heart rate (beats per min)	75 (13) [44 111]	78 (16) [48 144]
Prior Medications		
Diuretic	117 (86.7%)	120 (90.2%)
Beta Blocker	94 (69.6%)	108 (81.2%)
Angiotensin-Converting Enzyme Inhibitors	39 (28.9%)	45 (33.8%)
Angiotensin II Receptor Blockers	13 (9.6%)	7 (5.3%)
Angiotensin-Receptor Neprilysin	9 (6.7%)	11 (8.3%)
Hydralazine	11 (8.1%)	12 (9.0%)
Nitrate	19 (14.1%)	18 (13.5%)
If Channel Blocker	7 (5.2%)	9 (6.8%)
Digoxin	14 (10.4%)	18 (13.5%)

SMILE - Home Monitoring RCT



Presented by Dr. W. T. Abraham at HFSA, Philadelphia, Sep 2019

N = 224	Treatment (N=91)	Control (N=133)	HR	p-value	95% CI
Number of HF Readmissions	11	43	0.42	p = 0.01	[0.22-0.82]

- Statistical analysis: Anderson and Gill method
- Modified ITT population defined by
  - No ReDS measurements for > 20 consecutive days
  - No ReDS-guided treatment although > 8 threshold notifications sent
- Propensity analysis showed robustness of results
  - HR = 0.34, 95% CI [0.17-0.68], P = 0.002
- Note: since study was stopped early traditional ITT was not powered

ReDS-guided HF management when used as intended resulted in a significant 58% reduction in recurrent ADHF hospitalizations

SMILE Study Modified ITT Secondary Endpoint Results

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Time to First HF Readmission

N = 224	Treatment (N=91)	Control (N=133)	HR	95% CI	p-value
Number of HF Readmissions	10	34	0.51	0.25-1.03	p = 0.06

Proportion of Total Days Lost to HF Hospitalization

N = 224	Treatment (N=91)	Control (N=133)	Reduction	p-value
Proportion Total Days Lost to Hospitalization Due to HF Events (%)	0.6%	1.1%		
Average Per Patient (days)	1.02	2.06	50.4%	p = 0.02

Mortality

N = 224	Treatment (N=91)	Control (N=133)	p-value
All-cause Mortality	7	9	N.S.
CV Mortality	2	5	N.S.

Modified ITT Sensitivity Analysis

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Patient non-adherence	Non-adherence to ReDS-guided Protocol	Efficacy	p-value
No ReDS measurements for X consecutive days	No ReDS-guided treatment although more than X notifications were sent	HR	
>20 days	>4 notifications	**0.43**	0.01
>20 days	>8 notifications	**0.42**	0.01
>20 days	>16 notifications	**0.45**	0.02
>14 days	>4 notifications	**0.45**	0.02
>14 days	>8 notifications	**0.44**	0.01
>14 days	>16 notifications	**0.47**	0.02
>10 days	>4 notifications	**0.48**	0.03
>10 days	>8 notifications	**0.47**	0.03
>10 days	>16 notifications	**0.51**	0.04

Combinations of 10, 14 & 20 days with 4, 8 & 16 notifications show similar results: HR is between 0.42 to 0.51 --> 49% to 58% statically significant reduction in HF readmissions

Modified ITT Propensity Matched Analysis

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- Propensity scores were produced using baseline measures
- Nearest neighbor matching was used to identify a SOC group which was matched 1:1 with the modified ITT group to account for any baseline differences between the populations
- For completeness of the propensity model, all of the following baseline measures were included in the model:
  - Age
  - Gender
  - Race (White/Non-white)
  - Weight
  - Body Mass Index
  - Respiratory rate
  - HF etiology
  - History of CAD
  - Diabetes Mellitus
  - HFrEF vs. HFpEF
  - ACC/AHA Stage A, B vs. C, D
  - NYHA Class 1, 2 vs. 3, 4
  - Time from HF diagnosis
  - # of previous HF hospitalizations

Modified ITT Propensity Matched Results

The rate of recurrent events of HF readmissions during entire follow-up period (using A-G model)

N = 182	Treatment N=91	Control N=91	HR	p-value	95% CI
Number of HF Readmissions	11	36	0.34	0.002	0.17-0.68

Safety Analysis

- 422 reported Adverse Events
  - 87 were reported as Serious AEs

- None of the Adverse Events were related to the use of the Device
  - 5 *possibly* related
    - 4 – AKI, 1 – near Syncope
  - 4 *unlikely* related
    - 3 – Falls, 1 - asymptomatic orthostatic hypotension

Patients' Satisfaction

- ReDS arm patients filled satisfaction questionnaire
- The ReDS system got an average score of 4.5/5 in patient satisfaction

	Score 1-5
PSQ Questions - Scores range from 5 (strongly agree) to 1 (strongly disagree)	Treatment (N=135)
1. I am able to put the SensiVest on by myself.	4.7 ± 0.9 (92)
2. I was able to operate the SensiVest after one training session.	4.6 ± 1.0 (91)
3. I understood the training materials.	4.7 ± 0.8 (92)
4. The SensiVest is easy to use.	4.7 ± 0.8 (93)
5. The SensiVest worked reliably during the study.	4.4 ± 0.9 (92)
6. The SensiVest made me feel safer at home.	4.5 ± 0.9 (88)
7. The SensiVest saved me a trip to the hospital.	4.4 ± 1.2 (86)
8. The SensiVest saved me several trips to the hospital.	4.3 ± 1.1 (84)
9. I am more involved in my care when using the SensiVest.	4.3 ± 1.2 (90)
10. I learned more about my disease when using the SensiVest.	4.1 ± 1.2 (87)
11. I feel better about my health when I use the SensiVest.	4.4 ± 1.1 (91)
12. The call center is helpful.	4.5 ± 1.0 (86)
13. My doctor/NP can get a good understanding of my medical problem when I use the SensiVest.	4.7 ± 0.7 (90)
14. My doctor/NP uses information from the SensiVest during visits or telephone follow-ups.	4.8 ± 0.6 (86)
15. My doctor/NP used the information from the SensiVest to adjust my treatment and medications	4.5 ± 0.9 (85)
16. I would like to use the SensiVest in the future.	4.2 ± 1.3 (92)
17. I would recommend the SensiVest to other patients with the same medical condition.	4.6 ± 0.9 (92)
18. I feel more confident being active because I have a SensiVest.	4.1 ± 1.2 (88)
19. I like to be responsible of my own health.	4.8 ± 0.6 (91)
20. I like to take care of myself.	4.9 ± 0.5 (92)
Cells contain mean ± SD (N)	