DEPRESSION COGNITIVE BEHAVIORAL THERAPY TO IMPROVE HIV-CVD RISK: A PILOT RANDOMIZED CONTROLLED TRIAL

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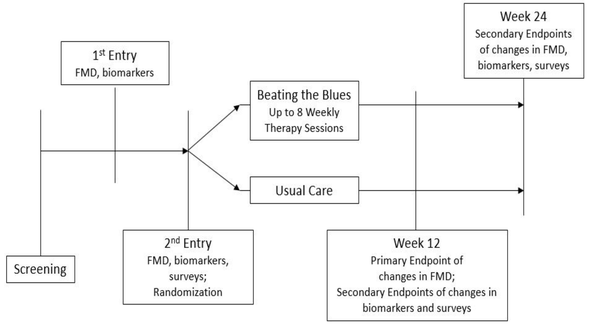
BACKGROUND

- CVD risk is higher in PLWH compared to HIV-negative people.
- Depression is common in PLWH and is associated with higher CVD risk and greater inflammation, especially monocyte activation, in the general population.
- We hypothesized that reducing depressive symptoms would causally improve CVD risk in PLWH.

METHODS

- We conducted a single-center, parallel-group, randomized, controlled, 24-week pilot trial comparing depression cognitive-behavioral therapy with usual care (UC).
- The intervention used was an internet depression CBT called Beating the Blues (BtB) US™. BtB involves 8 weekly one-hour sessions that are tailored to each patient's problems and includes challenging dysfunctional thoughts, activity scheduling, problem solving, sleep management, and relapse prevention.
- Participants were HIV+, ≥18 yrs, on ART for ≥1 yr, had VL<75c/mL, had PHQ-9 scores ≥10, and were without known CVD. Participants could receive any other depression therapy throughout the trial.
- Physiologic endothelial function was measured by brachial artery flow-mediated dilation (FMD), depressive symptom severity was assessed using PHQ-9 and SCL-20, and biomarkers of inflammation and coagulation were measured using standard ELISAs.
- Student's t-tests compared changes in endpoints at Weeks 12 and 24. Multiple imputation was used for missing FMD values.
- Pre-specified sensitivity analyses were performed comparing UC to BtB_{6-8}, a subgroup of the BtB assigned group who completed at least 6 of the 8 treatment sessions.

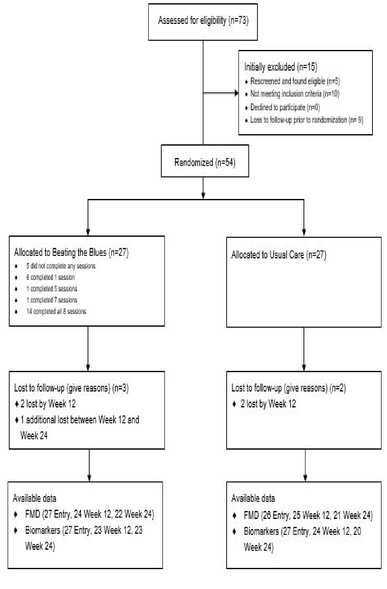


Study Design

Internet cognitive-behavioral therapy significantly reduces depressive symptoms and monocyte activation, but does not improve physiologic endothelial function, in PLWH on ART.

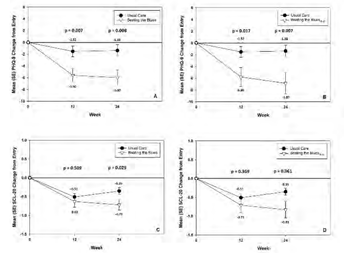
RESULTS

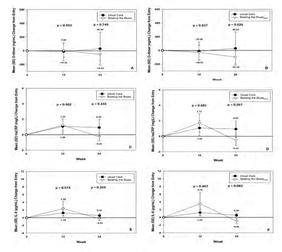
Participant Flow

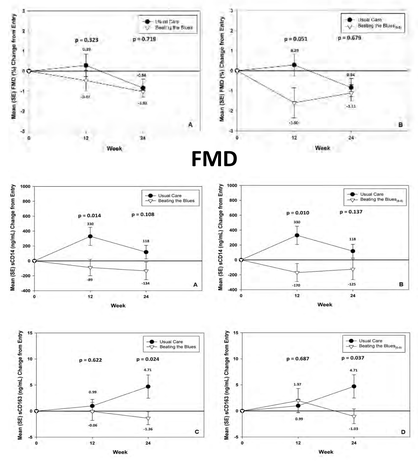


Baseline Characteristics

Characteristic	Usual Care (n=27)	Beating the Blues (n=27)	Beating the Blues$_{6-8}$ (n=15)	Total (n=54)
Age, years	45.6 (11.9)	44.6 (9.8)	47.5 (10.1)	45.1 (10.8)
Female sex	5 (19)	4 (15)	4 (27)	9 (17)
Black race	15 (56)	21 (78)	12 (80)	36 (67)
Current smoker	12 (44)	10 (37)	2 (13.3)	22 (41)
CD4 cell count, µL	743 (396)	713 (243)	760 (245)	728 (325)
Body mass index, kg/m^2	30.1 (6.7)	30.0 (7.0)	30.4 (8.7)	30.1 (6.7)
Systolic blood pressure, mmHg	123.5 (11.9)	127.7 (12.9)	127.3 (13.2)	125.6 (12.4)
Diastolic blood pressure, mmHg	77.7 (9.7)	80.0 (9.8)	78.4 (8.9)	77.4 (9.7)
Hemoglobin A1C, %	5.4 (0.7)	5.6 (0.5)	5.7 (0.6)	5.5 (0.6)
Estimated glomerular filtration rate, mL/min/1.73m^2	88.5 (23.5)	98.9 (18.4)	91.9 (17.2)	93.7 (21.5)
Triglycerides, mmol/L	1.27 (0.52)	1.44 (0.97)	1.48 (1.15)	1.35 (0.77)
Total cholesterol, mmol/L	5.02 (0.96)	4.83 (1.02)	5.02 (1.09)	4.92 (0.99)
High density lipoprotein-cholesterol, mmol/L	1.26 (0.34)	1.21 (0.38)	1.20 (0.43)	1.23 (0.36)
Low density lipoprotein-cholesterol, mmol/L	3.53 (1.00)	3.21 (1.05)	3.47 (1.09)	3.37 (1.03)
Glucose, mmol/L	5.77 (0.57)	5.73 (0.71)	5.79 (0.84)	5.75 (0.64)
Insulin, µU/mL	13.93 (10.48)	16.47 (16.25)	18.28 (19.89)	15.20 (13.60)
HOMA-IR	3.72 (2.90)	4.50 (5.00)	5.12 (6.22)	4.1 (4.1)
PHQ-9 score	14.0 (4.32)	17.13 (4.96)	17.13 (5.08)	15.6 (4.9)
SCL-20 score	2.09 (0.63)	2.27 (0.92)	2.27 (1.06)	2.18 (0.78)
Antidepressant medication use	19 (70)	18 (67)	10 (67)	37 (69)
hsCRP, mg/L	4.32 (3.84)	4.65 (4.46)	5.53 (5.02)	4.49 (4.12)
IL-6, pg/mL	2.59 (1.65)	2.80 (2.15)	3.76 (2.36)	2.69 (1.90)
D-dimer, ng/mL	2430 (845)	2536 (878)	2880 (882)	2483 (855)
Fibrinogen, µg/mL	2756 (756)	2707 (667)	2094 (770)	2731 (706)
sCD14, ng/mL	2233 (621)	2325 (849)	2302 (829)	2279 (732)
sCD163, ng/mL	43.30 (21.27)	46.61 (12.03)	50.77 (10.14)	44.86 (17.19)
sVCAM-1, ng/mL	378 (108)	375 (135)	367 (84)	376 (121)







CONCLUSIONS

- Compared to usual care, BtB (especially the BtB_{6-8} subgroup) was associated with clinically and statistically significant and persistent reductions in depressive severity symptoms through 24 weeks.
- FMD did not improve in either study group; in fact, there was a potential worsening of FMD at Week 12 with BtB_{6-8}, though this did not persist to Week 24.
- We did not find significant differences in D-dimer, hsCRP, or IL-6. However, BtB (especially in the BtB_{6-8} subgroup) was associated with significant improvements in the monocyte activation markers sCD14 and sCD163 compared to UC.
- This exploratory study was limited by a small sample size. We did not correct for multiple testing.
- Larger confirmatory trials are needed to determine if depression treatment leads to reductions in non-AIDS events linked to monocyte activation.

ADDITIONAL INFORMATION

- We thank the participants for their generosity. We also thank Ms. Danielle Huber, Ms. Jule Scott, Ms. Paula Johnson, Ms. Patricia Anderson, and Dr. Jessica Berntson for study coordination; Mr. Paul Sparks and Ms. Sheila Ellinger for regulatory assistance; and Dr. Robert Considine and Mr. Anthony Acton for performing the laboratory assays.
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