Fixed dose combination drugs for secondary prevention of cardiovascular disease among Syrian refugee and Lebanese patients attending MSF clinics in Lebanon

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Conflict of Interest:
The author has declared no conflict of interest.

Background

- 2 MSF primary care clinics in North Lebanon, 2012-2020 (Dar al Zahara (DAZ) and Abdeh clinics)
- Syrian refugees (majority) and local population
- Non-communicable disease (NCD) care included
- Cardiovascular disease (CVD) a common presentation

- ❖ non-specialist Lebanese general practitioners, supported by an international supervising specialist
- ❖ routine follow-up for stable patients provided by nurses; patients were seen by NCD doctor on at least every third visit and in case of complications
- ❖ Patient education provided by NCD nurses and doctors, and by health promotion staff
- ❖ appointment-based system for NCD consultations

Aims of the study

- Fixed-dose combination (FDC) drugs: cost-effective for primary and secondary prevention of CVD
    - Lack of use in low resource and humanitarian settings
- Aimed to assess whether FDC use is linked with *adherence* to CVD medications and *treatment simplification* in a humanitarian setting.
- Quantitative, qualitative and cost analysis components of study

Photos: Ghazal Sotoudeh/MSF

Ethics

This study was approved by the MSF Ethics Review Board, the LSHTM Research Ethics Committee, and the Lebanese American University's Institutional Review Board.

Specific informed consent was obtained from patients

Karine Pierre/Hans Lucas for MSF


Photo: MSF/Carole Al Farah

Methods

Patient eligibility

a) aged 18 years and older, attending DAZ or Abdeh MSF clinic,
b) with established atherosclerotic cardiovascular disease (history of coronary heart disease, ischaemic cerebrovascular disease, or peripheral artery disease) and
c) receiving (or eligible for) a multiple pill treatment regimen for secondary prevention (aspirin, statin, BP lowering medication)

- prospective, before-and-after cohort study
- patients enrolled February-May 2019
  - switched to Trinomia® FDC (atorvastatin 20mg, aspirin 100 mg, ramipril 2.5/5/10/mg) after six months' usual care
- two consecutive six-month periods of follow-up (before and after switch)

Key outcomes:

1. medication adherence (MARS-5)
2. non-high density lipoprotein cholesterol (non-HDL-C)
3. systolic blood pressure (SBP) control

- Checked at six and twelve months
- Descriptive and regression analyses
- intention-to-treat analyses and secondary analyses of non-switchers.

- *During the study, the Covid-19 pandemic, an economic crisis, and clinic closures occurred.*

Photos: Alla Karpenko/Jose Michelena/MSF

Results

521 enrolled patients

460 (88%) retention at 6 months;

418 (80.3%) switched to FDC

351 (84%) switched patients remained on FDC by month 12

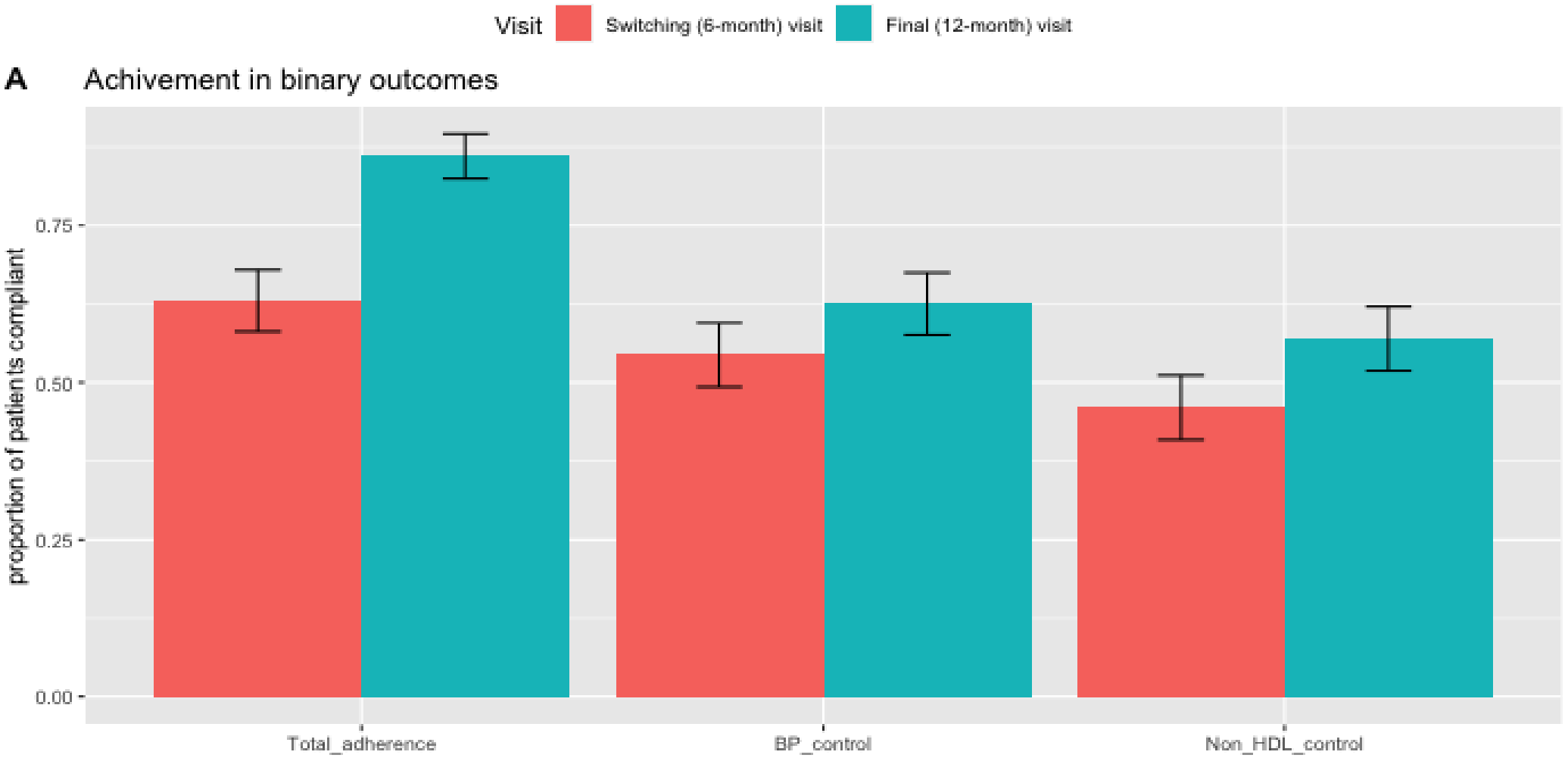
(8.1% (n=34) discontinued,

7.9% (n=33) lost to follow-up).

Photo: Jose Michelena/MSF

Results (2)

- 1. Total **adherence**: improved by 23% from 63% (95% confidence intervals (CI) 0.58-0.68) at month six to 86% (95% CI 0.82-0.90) at month 12.
    - those who were not fully adherent at 6 months had a 78.8% chance of improved adherence by 12 months
- 2. Mean **SBP**: dropped 3.07 mmHg (95% CI -4.76 to -1.38; p= 0004) from 132.7 (95% CI 130.8 - 134.6) to 129.7 mmHg (95% CI 127.9 - 131.5).
    - Control improved from 54% [49-60%] to 63% [58-68%] at 12 months
- 3. Mean **non-HDL-C** levels dropped 0.28 millimoles/litre (mmol/L; 95% CI -0.38 to -0.1; p=0.000) from 2.39 (95% CI 2.26 - 2.51) to 2.11 mmol/L (95% CI 2.00 - 2.22)
    - Control improved from 46% (95% CI 41-51%) to 57% (95% CI 52-62%)


Visit
Switching (6-month) visit
Final (12-month) visit
A
Achivement in binary outcomes
proportion of patients compliant
0.75
0.50
0.25
0.00
Total_adherence
BP_control
Non_HDL_control

Qualitative component

Patients

- Overall positive experience: **“one pill is easier than separate pills”**
- Few patients expressed fear or reluctance related to an unfamiliar drug; few patients expressed having some minor side effects
- Majority would have continued using the FDC if MSF clinics had remained open

MSF Staff

- Overall positive perception; felt it was an improvement in treatment and facilitated patient adherence
- Overall reduction in work burden
- Majority believed it could be used in other MSF clinics in Lebanon, but were uncertain if this could be scaled up in other PHCs in the country

Limitations

- relatively small numbers of patients
- before and after cohort study rather than randomised blinded controlled trial
- possible lack of scalability in Lebanon's public health system – MSF's structured multi-disciplinary clinic not representative

Photo: Sophie Wodon/MSF

Conclusion

- use of a CVD secondary prevention FDC is feasible and effective in a humanitarian setting
- acceptability by patients and providers demonstrated in a qualitative component of this study
- costs of this approach have also been investigated and pending analysis
- higher proportion may reach non-HDL-C targets with use of a high intensity statin dose
- further work needed to determine how an FDC for hypertension could be combined with a CVD secondary prevention FDC and, potentially, with FDCs containing combinations of oral hypoglycaemic drugs
- Like FDCs for HIV, this could enable:
  - Improved tolerability and adherence,
  - simplification of treatment regimens, and
  - An improved public health approach to management including community-based management by non-physician health workers
- Potential to help address large gap in use of secondary prevention medications in those at high risk of CVD, especially in low resource and humanitarian settings

MEDECINS SANS FRONTIERES

SCIENTIFIC DAYS

Acknowledgments

- MSF Switzerland Lebanon team
- LSHTM collaborating partners
- Participants in the study

Photos: MSF/Carole Al Farah