Colchicine for prevention of post-pericardiotomy syndrome and post-operative atrial fibrillation: the COPPS-2 randomized clinical trial.

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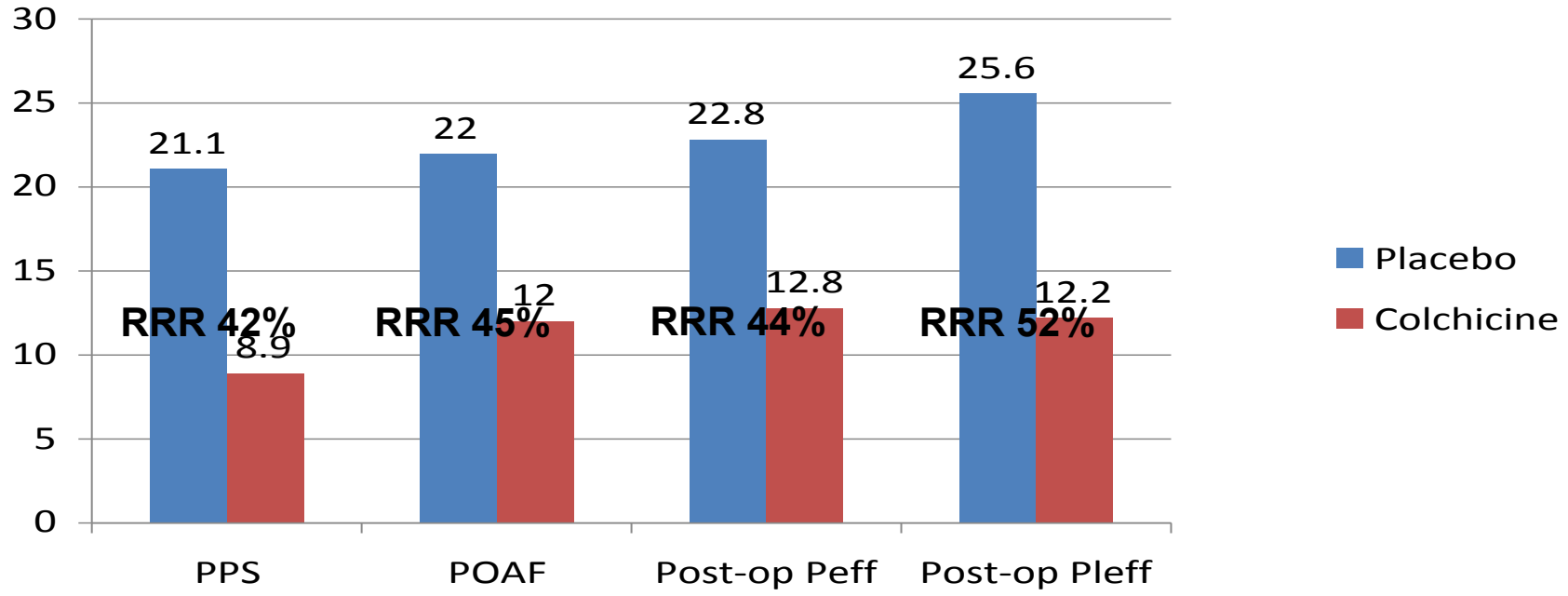
Disclosures:

- The COPPS-2 trial was supported by former Azienda Sanitaria 3 of Torino (now ASLTO2) within the Italian National Health Service.
- Acarpia (Madeira, Portugal) provided the study drug and placebo as an unrestricted institutional grant and had no role in planning of the study, analysis of data, or writing of the manuscript.
- FAR.G.IM. srl (Catania, Italy) provided funding to support insurance costs for the trial.

Unlabeled use of drugs:

- Colchicine for PPS and POAF prevention

Background: COPPS Trial



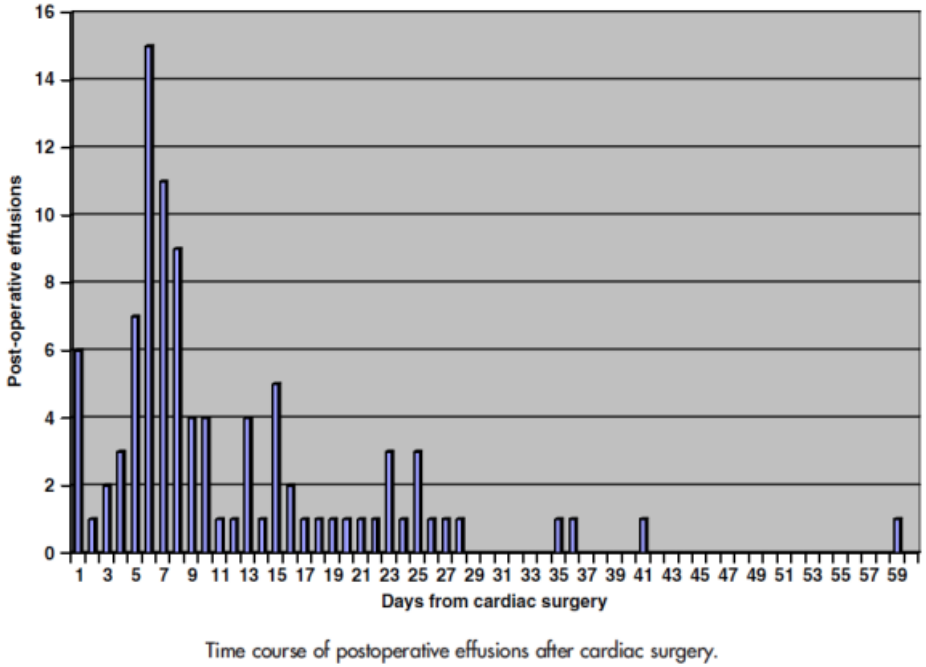
180 vs. 180 pts 167 vs. 169 pts 180 vs. 180 pts

Eur Heart J. 2010 Nov;31(22):2749-54
Circulation. 2011 Nov 22;124(21):2290-5
Am Heart J. 2011 Sep;162(3):527-32.e1

PPS and POAF

COPPS: PPS incidence

90% in 60 days

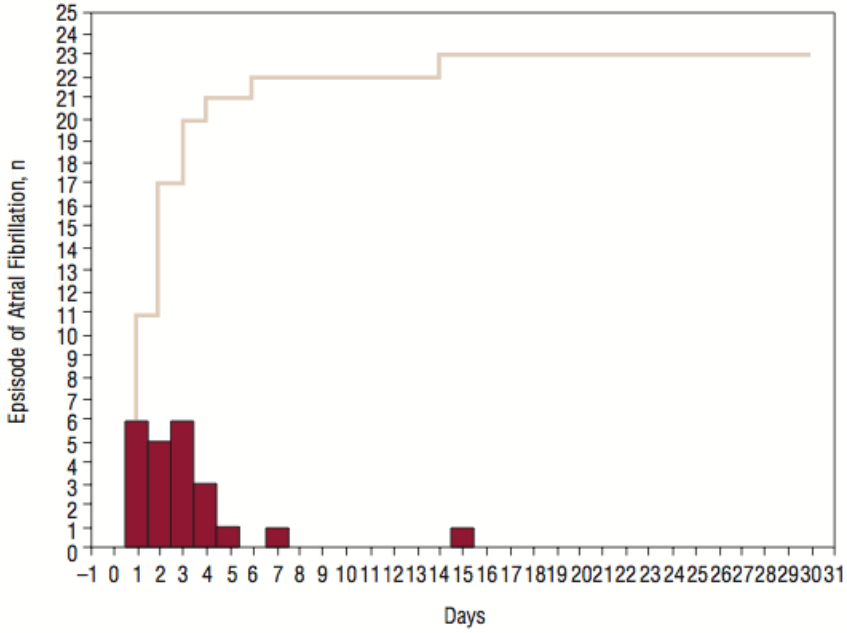


Time course of postoperative effusions after cardiac surgery.

Am Heart J. 2011 Sep;162(3):527-32.e1.

POAF incidence

70% POAF in ICU



Rev Esp Cardiol. 2007;60(8):841-7

COPPS vs. COPPS-2

Feature	COPPS	COPPS-2
Main objective	To evaluate the efficacy and safety of colchicine for the primary prevention of the post-pericardiotomy syndrome following cardiac surgery.	To determine whether perioperative use of oral colchicine is efficacious and safe for prevention of post-pericardiotomy syndrome, post-operative AF, and post-operative effusions.
Design	Multicenter, double blind RCT	Multicenter, double blind RCT
Setting	6 centers in Italy	11 centers in Italy
Participants	360 patients after cardiac surgery	360 candidates to cardiac surgery
Intervention	Placebo or colchicine started on the third post-operative day. Colchicine was given at the dosage of 1.0 mg twice daily for the first day followed by a maintenance dose of 0.5 mg twice daily for 1 month in patients ≥70 kg, and halved doses for patients <70 kg or intolerant to the highest dose.	Placebo or colchicine (0.5 mg twice daily in patients ≥70 kg or colchicine 0.5 mg once daily in patients weigthing less) between 48-72 hours before surgery and continued for 1 month after surgery.
Primary outcome	Incidence of the PPS at 12 months	Occurrence of post-pericardiotomy syndrome within 3 months.
Main secondary end points	Combined rate of disease-related hospitalization, cardiac tamponade, constrictive pericarditis, and recurrent pericarditis.	Occurrence of postoperative AF and effusions within 3 months.
Substudy	COPPS-POAF (336 patients in sinus rhythm before starting the intervention after cardiac surgery to test the efficacy and safety of colchicine for the prevention of POAF after cardiac surgery.	None

Am Heart J. 2013 Jul;166(1):13-9

Objective

- To determine the efficacy and safety of perioperative administration of oral colchicine to reduce:

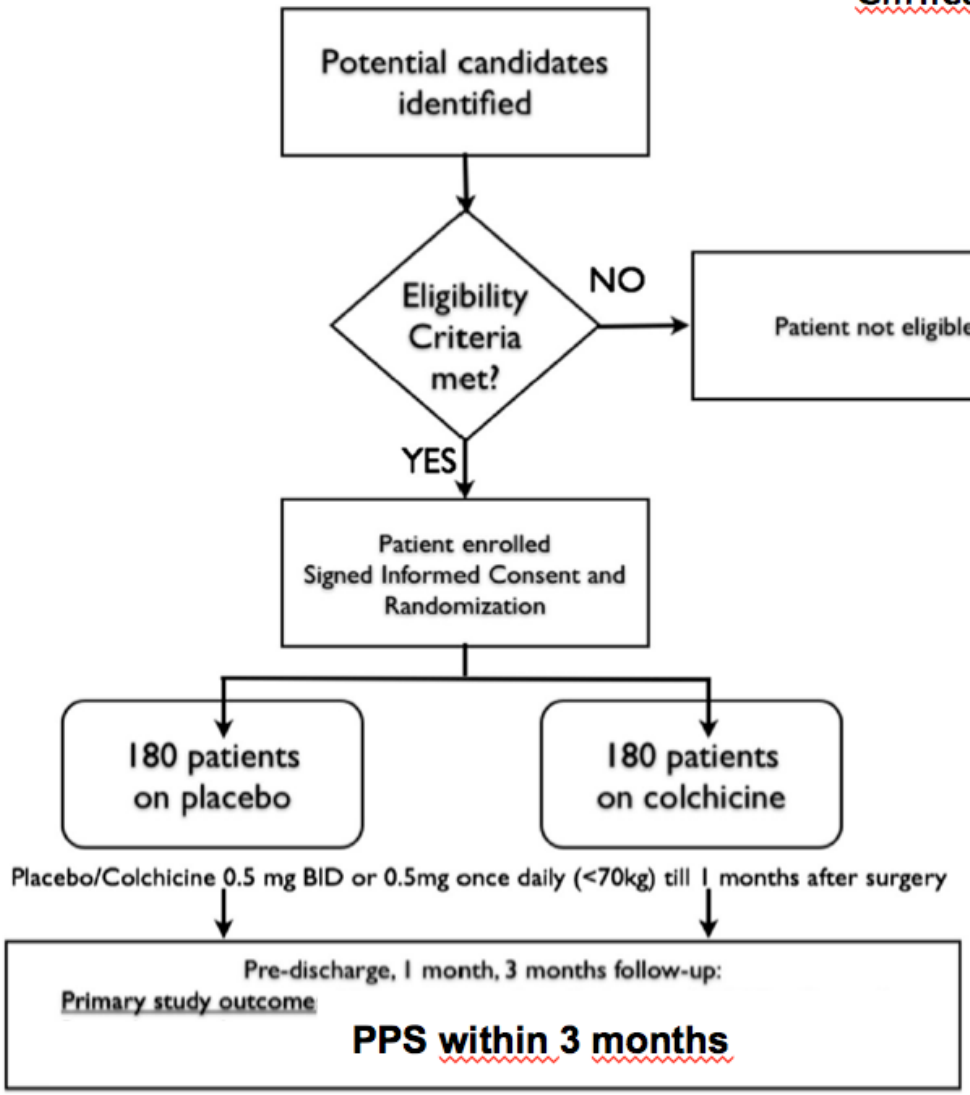
➢ post-pericardiotomy syndrome (PPS),

➢ post-operative AF (POAF),

➢ post-operative effusions (pleural and/or pericardial).

Design, Setting, Participants, Intervention

ClinicalTrials.gov Identifier: NCT01552187



Inclusion and exclusion criteria

Inclusion criteria
- Age >18 y
- Candidate to cardiac surgery
- Informed consent

Exclusion criteria
- Current atrial fibrillation
- Candidate to cardiac transplantation
- Severe liver disease or elevation of serum transaminases (>1.5 times the upper reference limit)
- Serum creatinine >2.5 mg/dL
- Preoperative elevation of CK or known myopathy
- Known chronic intestinal diseases or blood dyscrasias
- Pregnancy, lactation, or women of childbearing potential not protected by a contraception method
- Hypersensitivity to colchicine
- Treatment with colchicine for any cause

Preoperative elevation of CK beyond upper limit of reference interval.

Main Outcome Measures

PPS within 3 months (primary end point):

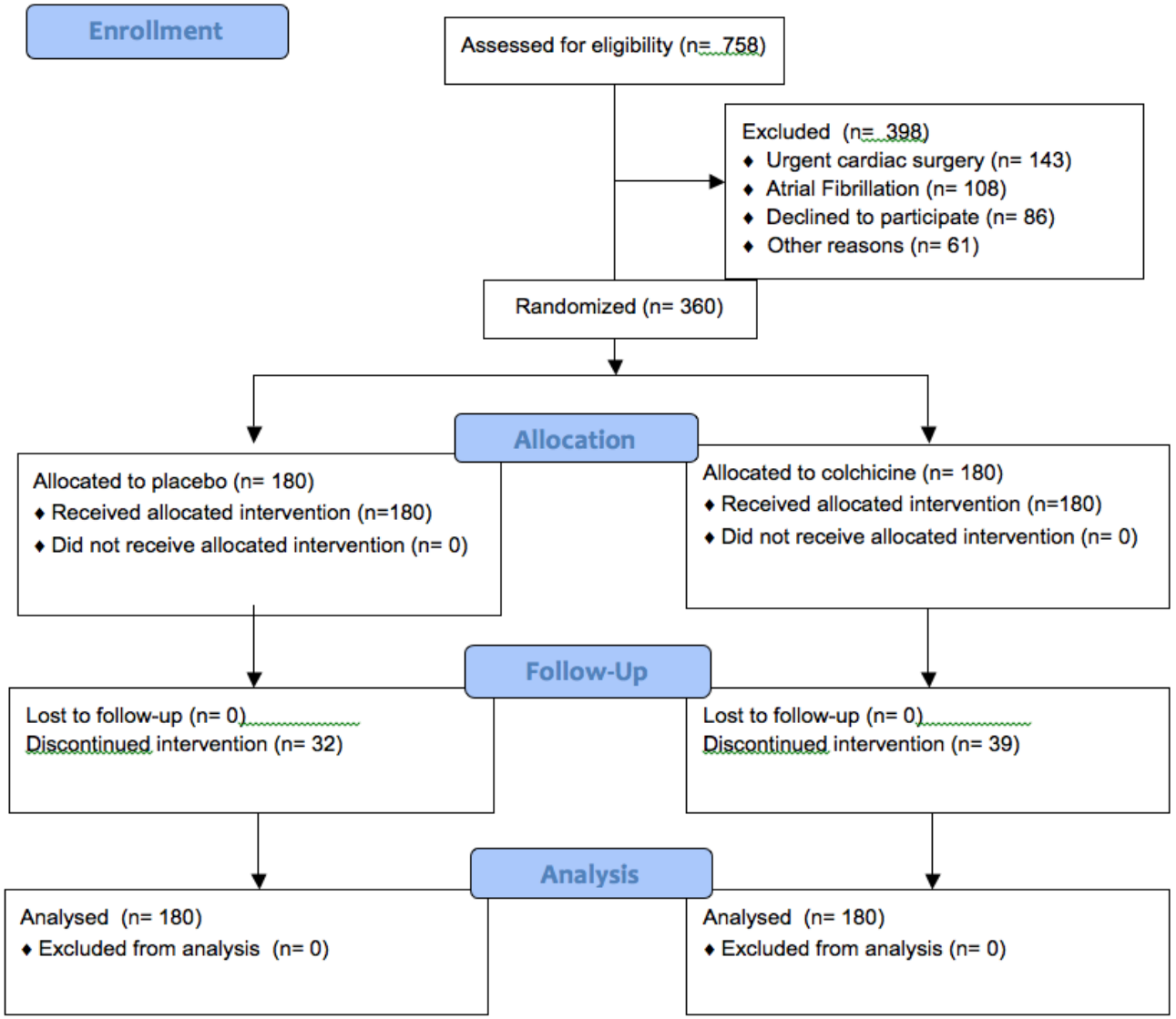
At least 2 of these criteria should be present for the diagnosis

1. Fever without alternative causes
2. Pleuritic chest pain
3. Friction rub
4. Evidence of new or worsening pleural effusion
5. Evidence of new or worsening pericardial effusion

POAF within 3 months (secondary end point):
Post-operative AF was defined as AF lasting for more than 30 seconds. Continuous ECG monitoring at least 5 days post-surgery then daily ECG and symptoms-guided.

Post-operative eff. within 3 months (secondary end point):
Pericardial and/or Pleural by ultrasonography.

Study Flow diagram

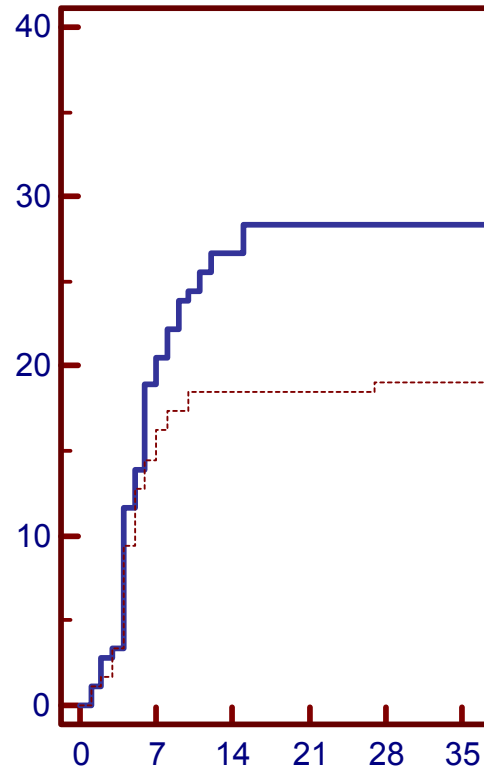


Baseline Data

Results

Kaplan-Meier incidence of post-pericardiotomy syndrome according to treatment groups.

Log-rank p=0.046



Number at risk

Group: Placebo						
	180	143	131	128	128	128
Group: Colchicine						
	180	147	141	141	139	139

Safety

Feature	Placebo (n=180)	Colchicine (n=180)	Absolute differences (95% CI) %
Adverse events	21 (11.7%)	36 (20.0%)	8.3 (0.76 to 15.9)
Gastrointestinal intolerance*	12 (6.7%)	26 (14.4%)	7.7 (1.4 to 14.3)
Hepatotoxicity°	2 (1.1%)	1 (0.6%)	0.50 (-2.1 to 3.4)
Drug discontinuation	32 (17.8%)	39 (21.7%)	3.9 (-4.4 to 12.5)

Reported data represent the number of affected individuals.
No serious adverse events (any fatal or life-threatening event, requiring hospitalization, or significantly or permanently disabling or medically significant, that could have jeopardized the patient or required medical or surgical intervention to prevent an adverse outcome) were reported, as well as myotoxicity, alopecia or other side effects beyond those reported in the table.
*= Diarrhea, nausea, cramping, abdominal pain, or vomiting.
°= Any elevation of aminotransferase levels above the normal reference range.

Conclusions

- Among patients undergoing cardiac surgery, the perioperative use of colchicine compared with placebo reduced the incidence of post-pericardiotomy syndrome but not of post-operative AF or postoperative effusions.
- The increased risk of gastrointestinal adverse effects reduced the potential benefits of colchicine in this setting.

Acknowledgment: COPPS-2 Investigators

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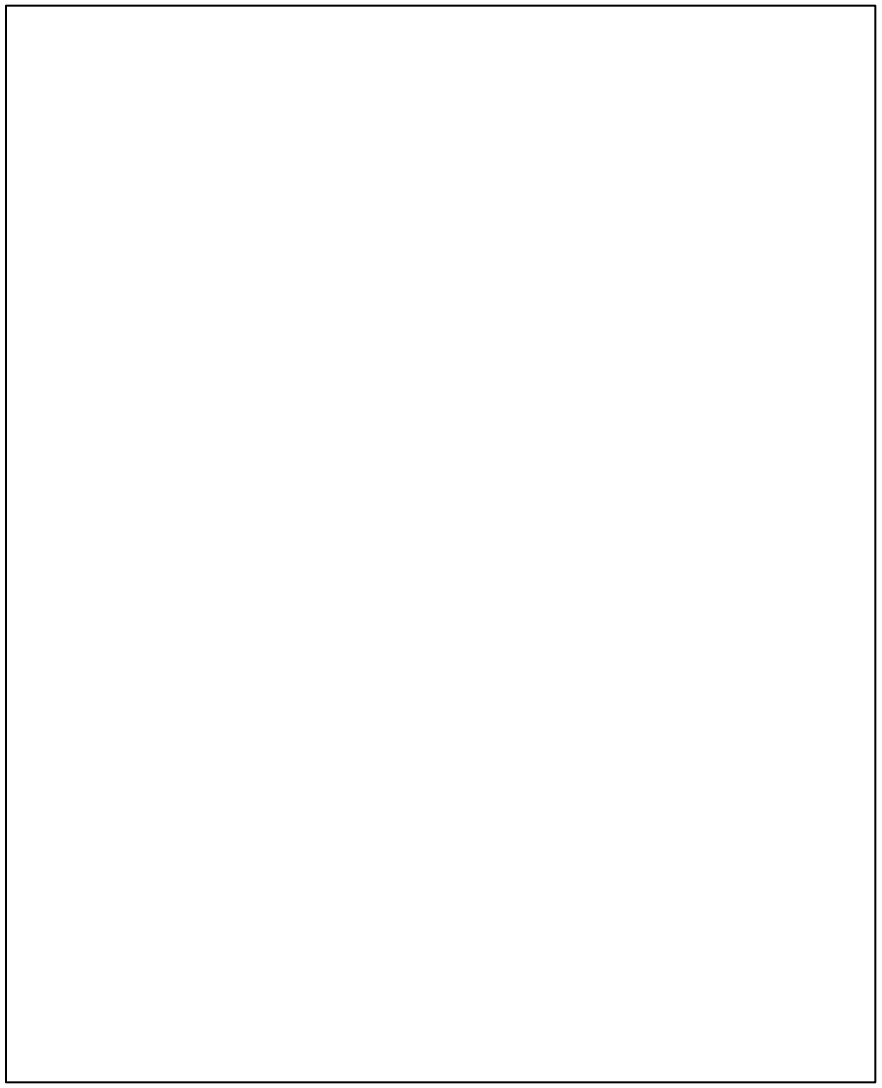

JAMA®

The Journal of the American Medical Association

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Published online August 30, 2014

Available at jama.com and on The JAMA Network Reader at mobile.jamanetwork.com

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