Collaboration with Cardiology The Oncologists' Perspective and Needs

Moderator: Durand
Panelists: Susan Dent, MD, FRCPC and. Weiss

February 18th, 2017

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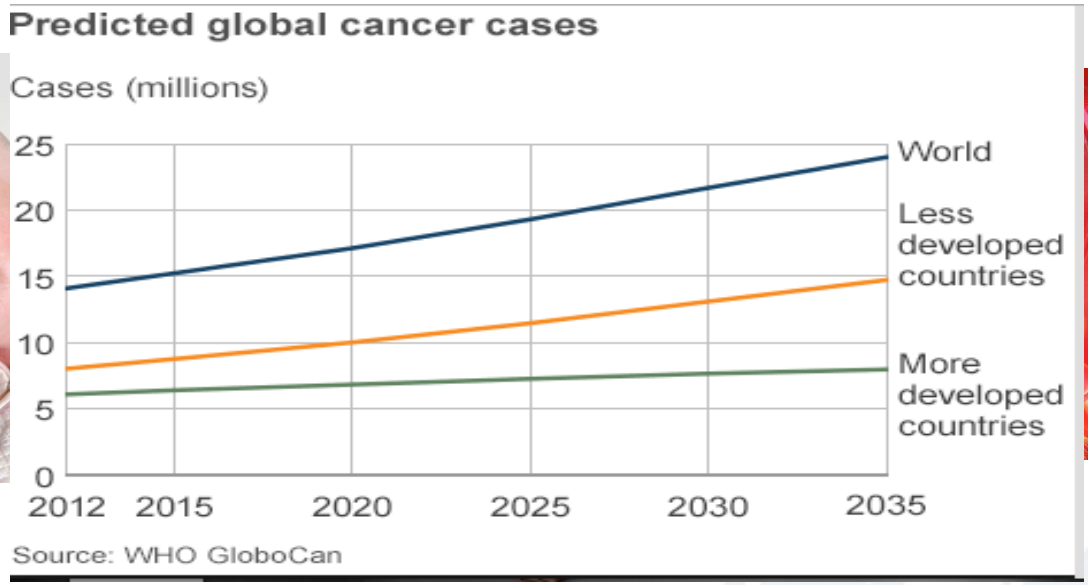

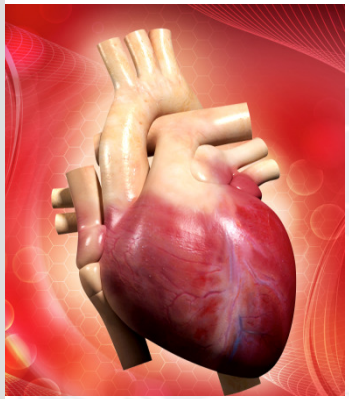

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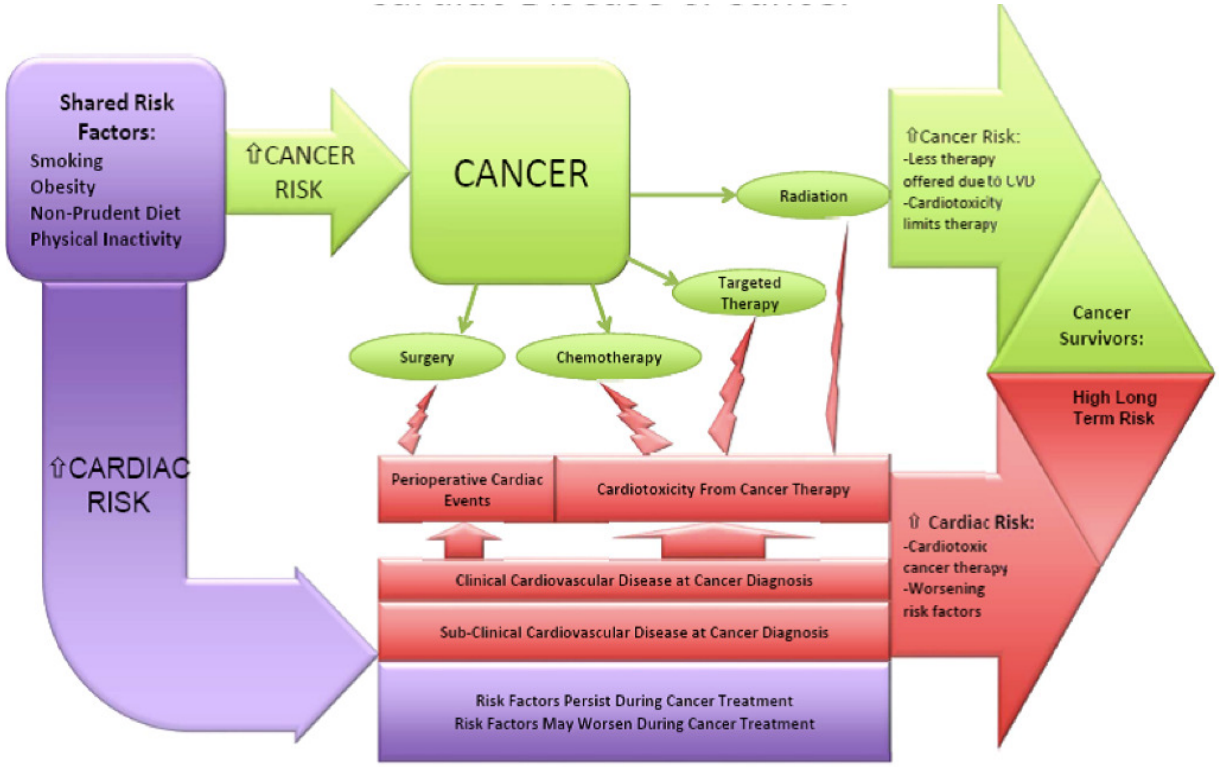
Cancer and Heart Disease – Common Risk Factors



C. Johnson et al. Can. Journal of Cardiology 2016

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Case Study: Mrs. B.R

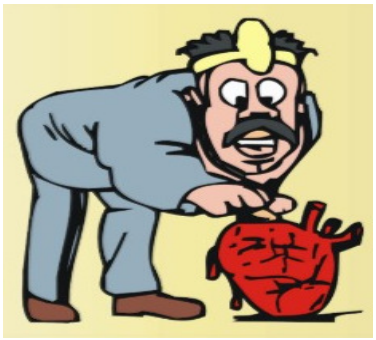
- 75 y.o post-menopausal women seen by the oncologist with a recent diagnosis of stage I breast cancer : ER +/PR -/ HER2 +
- Oncologist recommends adjuvant systemic therapy with weekly paclitaxel x 12 and trastuzumab q 3 weeks x one year; radiation and the endocrine therapy (aromatase inhibitor) x 5 years
- Baseline echo: LVEF= 50 % (borderline)
- PMH
  - atrial fibrillation x 10 years – on coumadin with stable INR (2.2)
  - Borderline hypertension (160/95) (at home 140/90)
  - hypercholesterolemia
  - Meds: coumadin, metoprolol (rate control), lipitor

Oncologists Perspective

- Should I be concerned about her cardiac risk factors?
- Is it safe to treat her with chemotherapy/trastuzumab/aromatase inhibitors?
- Are there any preventative strategies we could use?
- What about coumadin? Would you switch her to a NOAC?

Cardiologist Perspective

- What is her risk of breast cancer recurrence?
- Is trastuzumab a necessary component of her cancer treatment?
- Given her cardiac risk factors would tamoxifen be a reasonable choice for endocrine therapy vs an aromatase inhibitor?
- Are there any differences in Selective vs Non-Selective Beta Blockers?



Optimize Cardiac Health

Best Cancer Care

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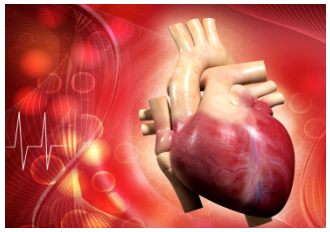
What we don't know….



- Long term sequelae of modern cancer agents in non – clinical trial patients (registry data)
- Cardiotoxicity in patients exposed to multiple cancer drugs
- Cardiac monitoring long term (survivors)
- Monitoring of patients on long term cancer therapy (e.g pertuzumab/trastuzumab in metastatic breast cancer)
- If cardiac medication (primary prevention) is started when do you stop ?

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Save the Date

Global Cardio-Oncology Summit 2017

September 20-21, 2017
London, UK

Additional details to follow.

British Cardio-Oncology Society
BC-OS.org

Canadian Cardiac Oncology Network

INTERNATIONAL CardiOncology SOCIETY

British Cardiovascular Society

WE ARE MACMILLAN. CANCER SUPPORT

Royal Brompton & Harefield NHS
NHS Foundation Trust

Topics include:

- How to deliver a Cardio-Oncology service
- Training in Cardio-Oncology
- eHealth and Cardio-Oncology
- How do I measure the quality of my service?
- Role of primary care in cancer survivors
- Immunotherapy and emerging cardiotoxicity
- Personalised medicine & genetics
- EP session –who should have ablation, ICDs, CRT?
- Anticoagulation and antithrombotic (AF, ACS)

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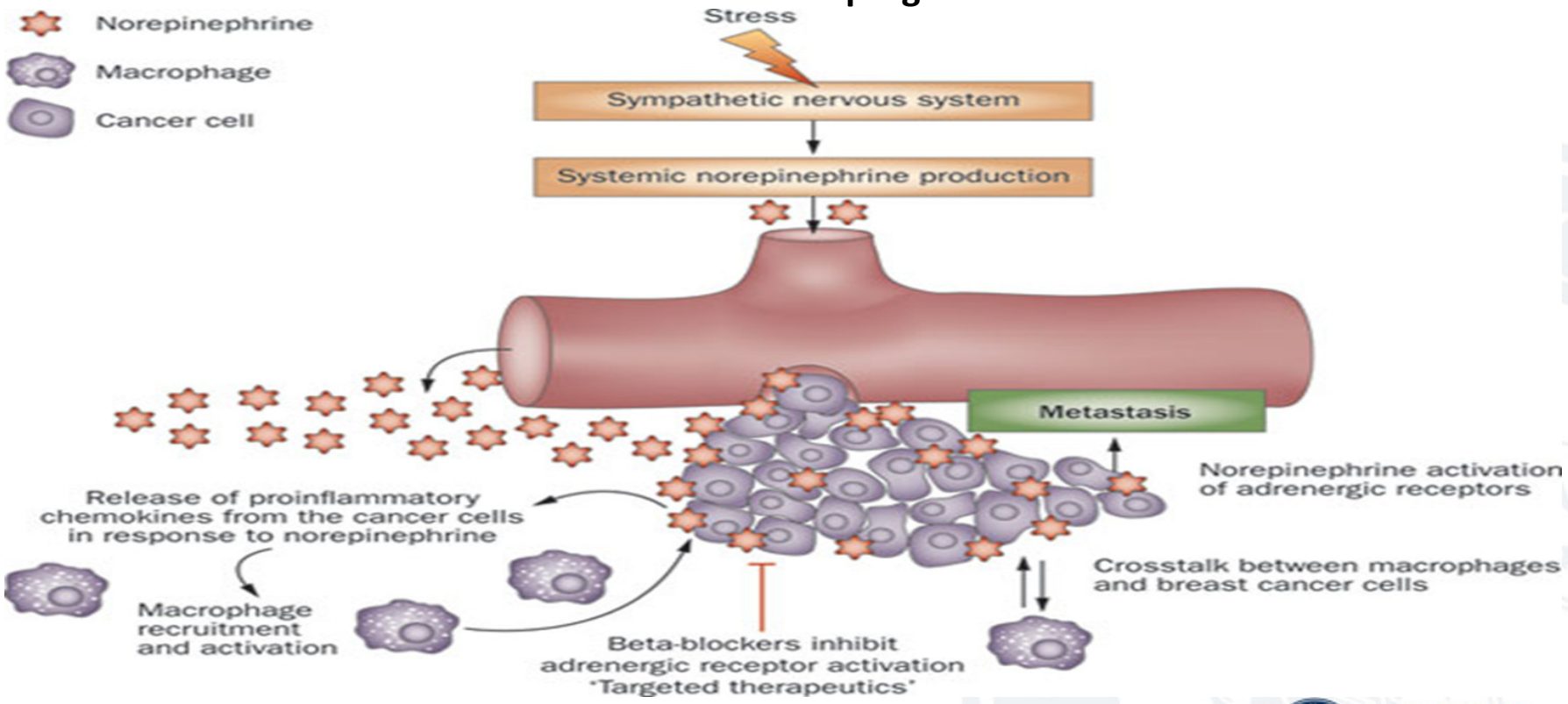
Binding to specific adrenergic receptors, β-blockers inhibit cancer cell migration and metastasis, suggesting a novel targeted therapeutic application in protecting against breast cancer disease progression



Powe, D. G. & Entschladen, F. Nature Reviews Clinical Oncology 8, 511-512 (2011

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Triple Negative and Estrogen Receptor Positive outcomes

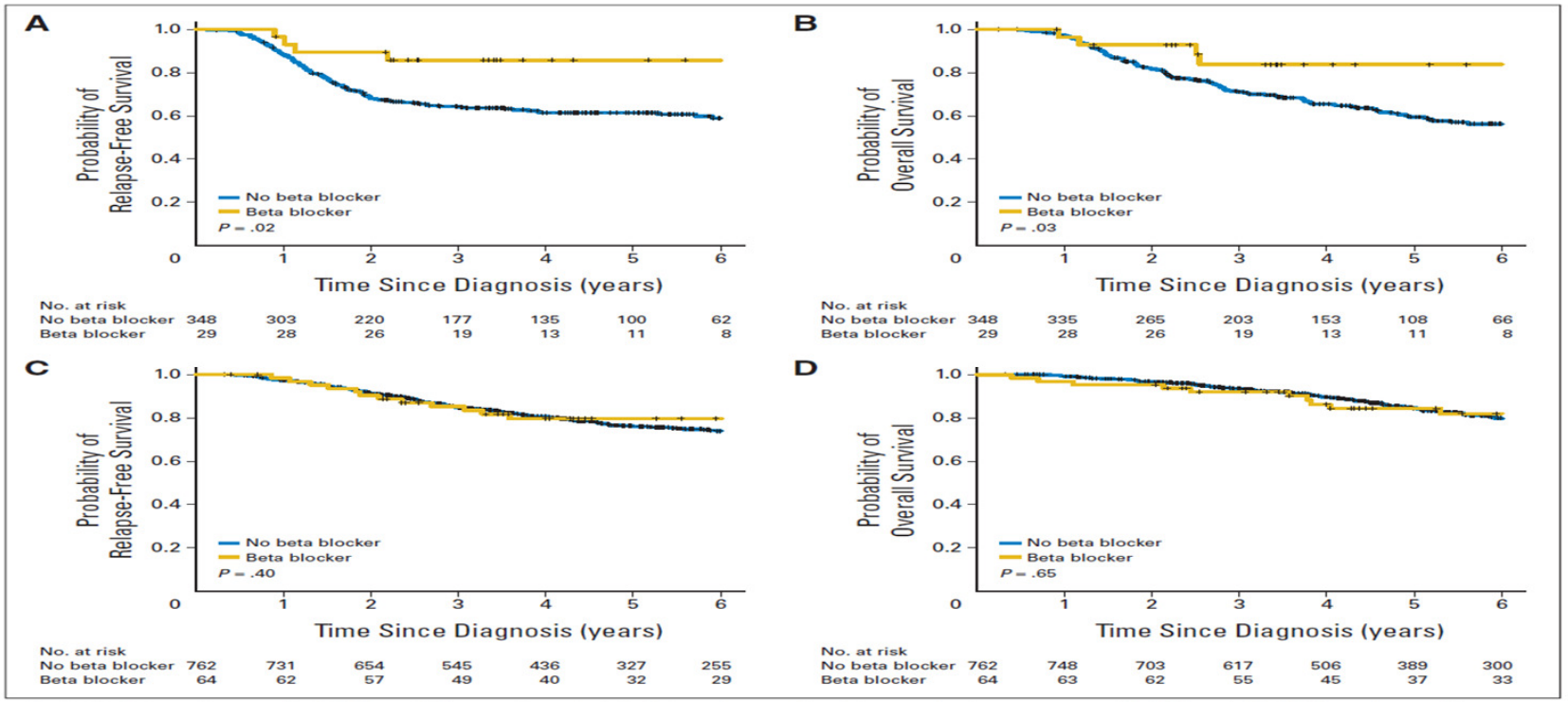

Fig 1. (A) Relapse-free survival (RFS) and (B) overall survival (OS) in patients with triple-negative breast cancer. (C) RFS and (D) OS in patients with estrogen receptor–positive breast cancer.

J Clin Oncol 29;2645-2652

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Baseline Hypertensive BC Patients Treated with Beta Blockers Live Longer

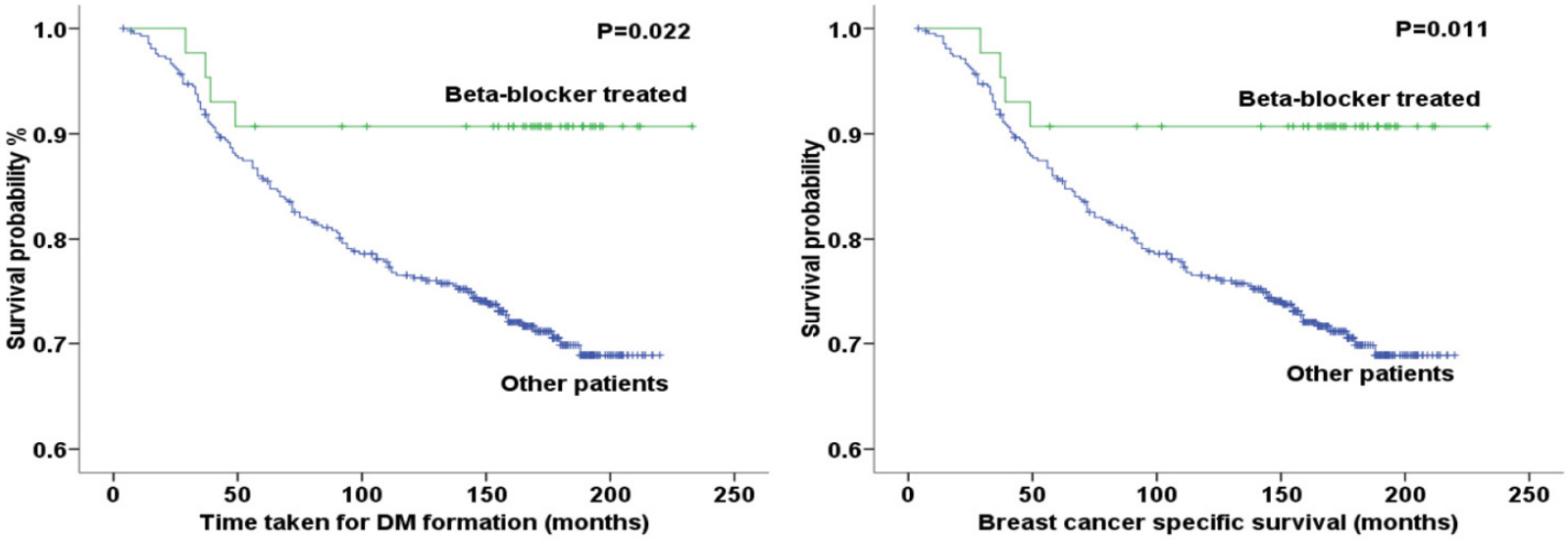

Figure 1a: Hypertensive BC patients therapeutically treated with beta-blockers showed significantly (p=0.022) longer times before acquiring metastases compared to non-treated patients.

Figure 1b. Hypertensive BC patients receiving beta-blocker therapy showed significantly (p=0.011) improved 10 year survival rates compared to non-treated patients.

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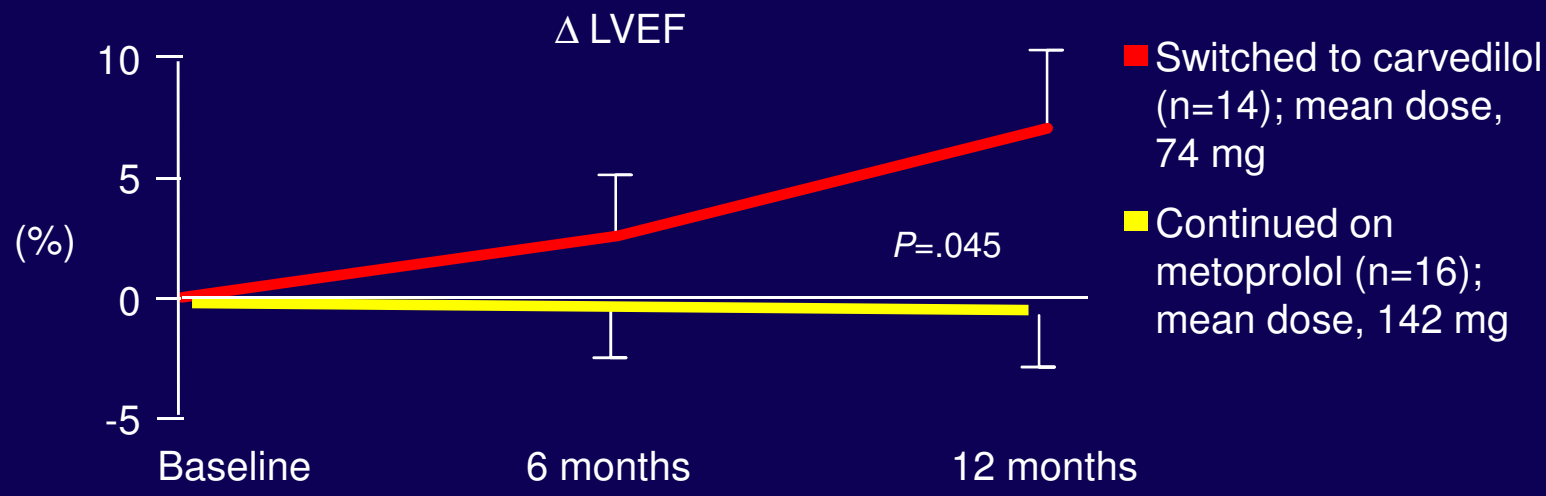
Oncotarget 2010; 1:628-638

Effects of Carvedilol in Patients With Persistent LVD Despite Continuous Metoprolol



- At 12 months, carvedilol patients had mean EF increase of 7 units vs -0.8 units in metoprolol patients

Open-label randomized study of IDC patients with EF <40% on long-term metoprolol (>1 year).
Patients receiving ACE inhibitors; follow-up 12 months.

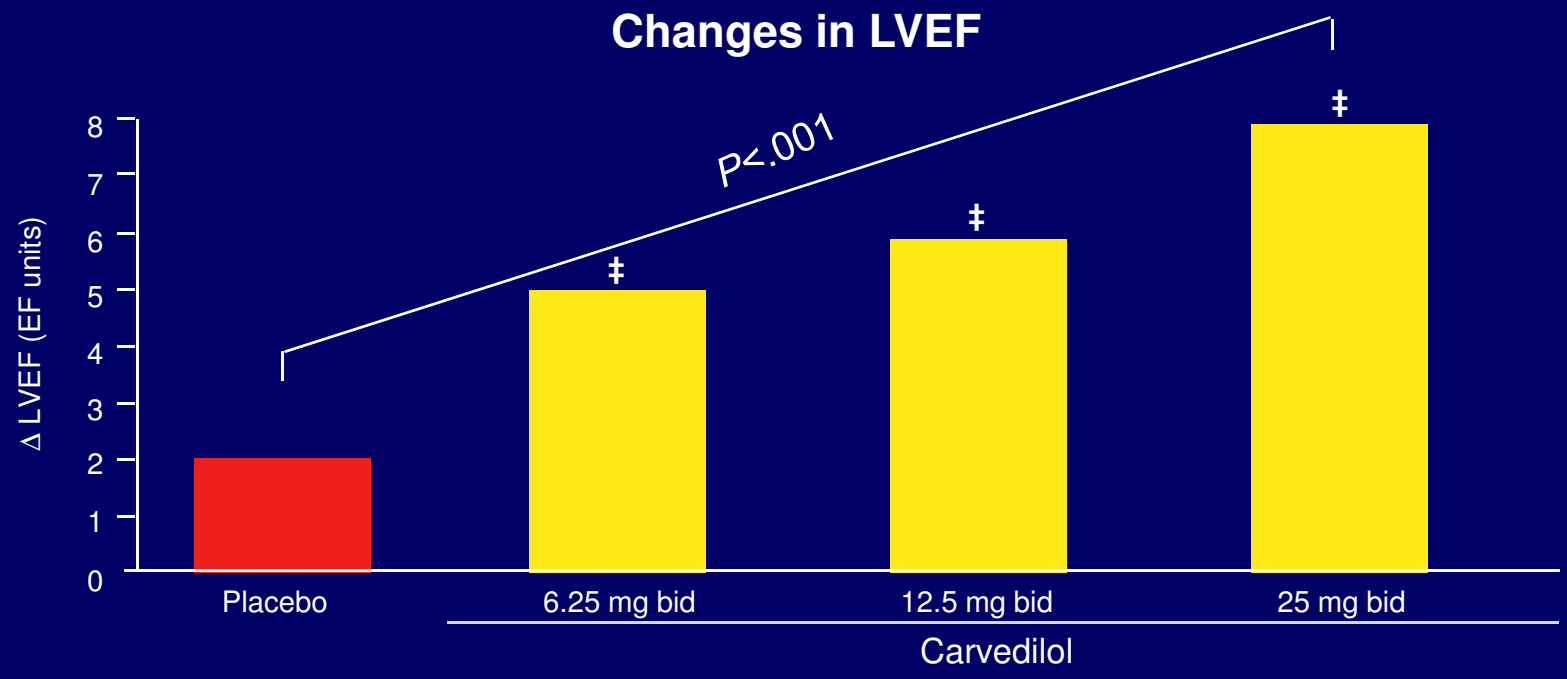
Di Lenarda et al. J Am Coll Cardiol. 1999;33:1926-1934.

Major Trials of β-Blockade in Heart Failure

	Patients (n)	Follow-up (yrs.)	Target dose (total/day)	Mean dose achieved (total/day)	Effects on outcomes
CIBIS	641	1.9	5 mg	3.8 mg	All-cause mortality: NS
CIBIS-II	2647	1.3	10 mg	7.5 mg	All-cause mortality: ↓34% (*P*<.0001)
MDC	383	1	100 to 150 mg	108 mg	Death or need for transplant (primary endpoint): NS
MERIT-HF	3991	1	200 mg	159 mg	All-cause mortality: ↓34% (*P*=.0062)
US Carv trials†	1094	7.5 mo.	50 to 100 mg	45 mg	All-cause mortality*: ↓65% (*P*=.0001)
ANZ Trial	415	1.5	50 mg	41 mg	Death or all-cause hospitalization: ↓26% (*P*=.02)

*Not a planned endpoint.
†Carvedilol is the only agent approved by the FDA for the treatment of mild to moderate heart failure.

Carvedilol Dose-Response Trial (MOCHA*): Effect on Ejection Fraction and Mortality



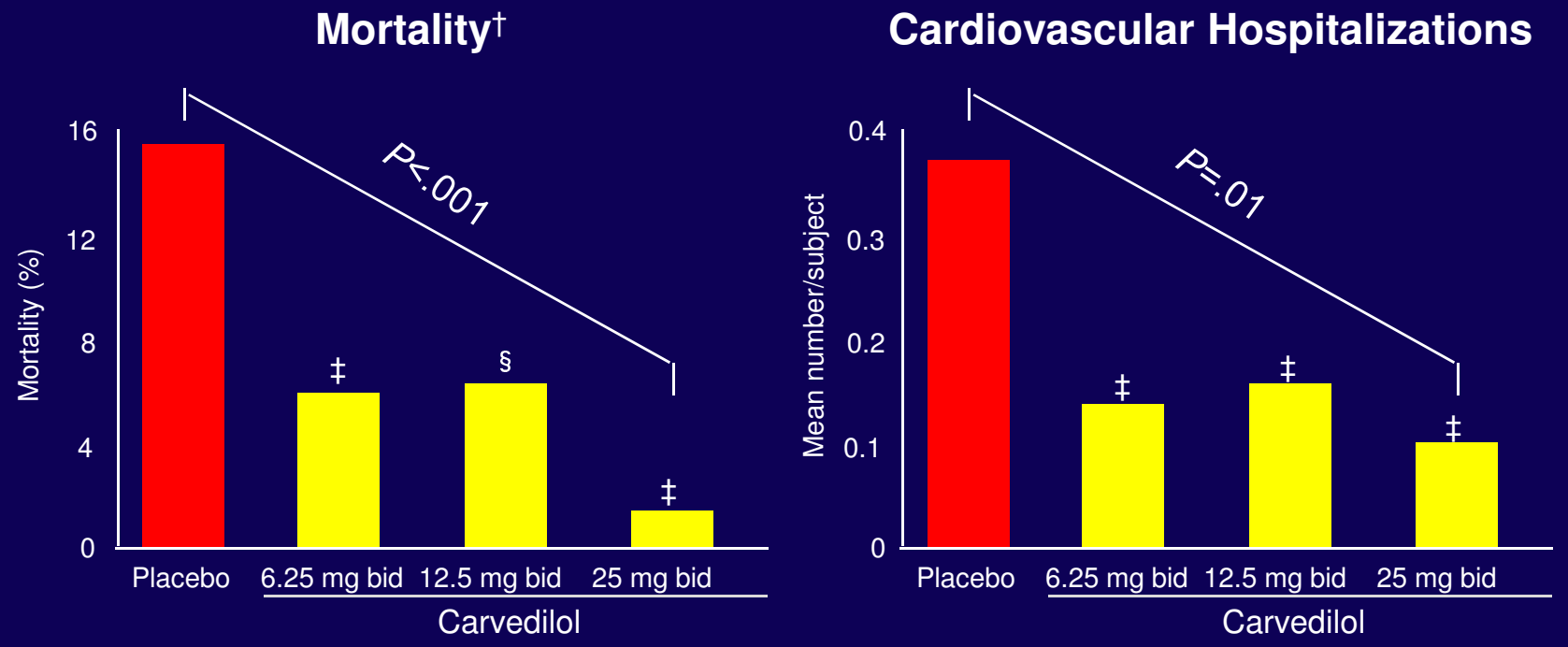
Patients receiving diuretics, ACE inhibitors, ± digoxin; follow-up 6 months; placebo (n=84), carvedilol (n=261).

*Multicenter Oral Carvedilol Heart Failure Assessment.

‡*P*<.05 vs placebo.

Adapted from Bristow MR et al. *Circulation*. 1996;94:2807–2816.

Carvedilol Dose-Response Trial (MOCHA*): Effect on Mortality and Morbidity



Patients receiving diuretics, ACE inhibitors, ± digoxin; follow-up 6 months; placebo (n=84), carvedilol (n=261).

*MOCHA, Multicenter Oral Carvedilol Heart Failure Assessment.

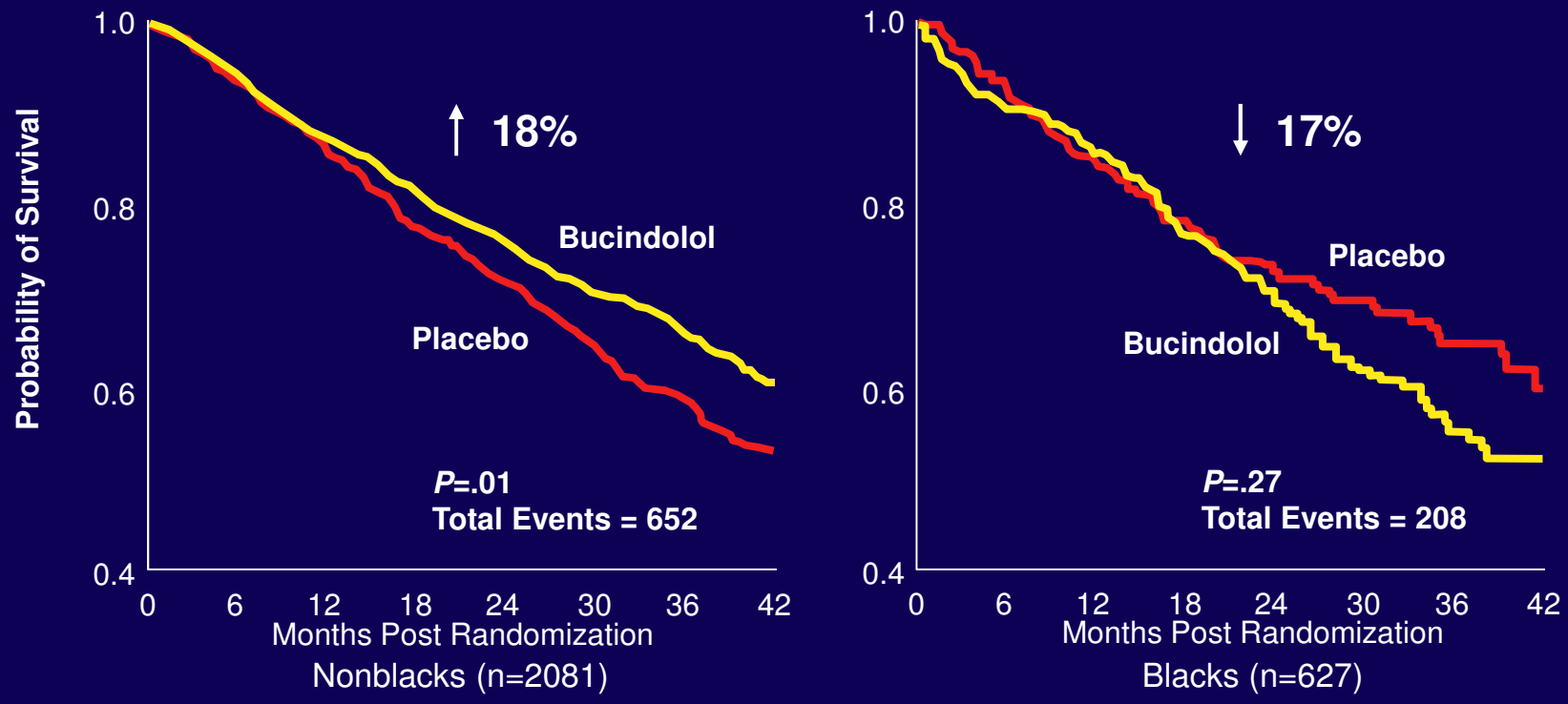
†Mortality was not a planned endpoint in this study.

Adapted from Bristow et al. Circulation. 1996;94:2807-2816.

‡$P<.05$ vs placebo.

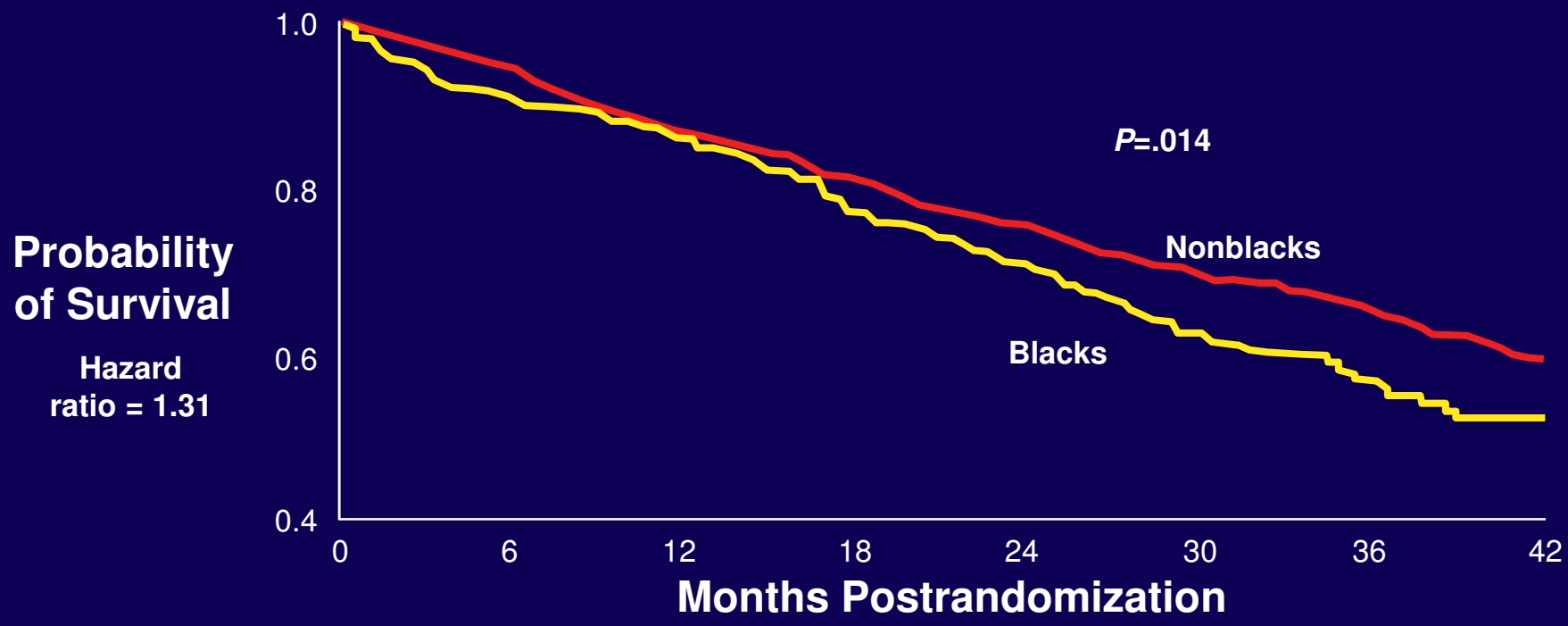
§ $P=.07$ vs placebo.

BEST: All-cause Mortality by Race



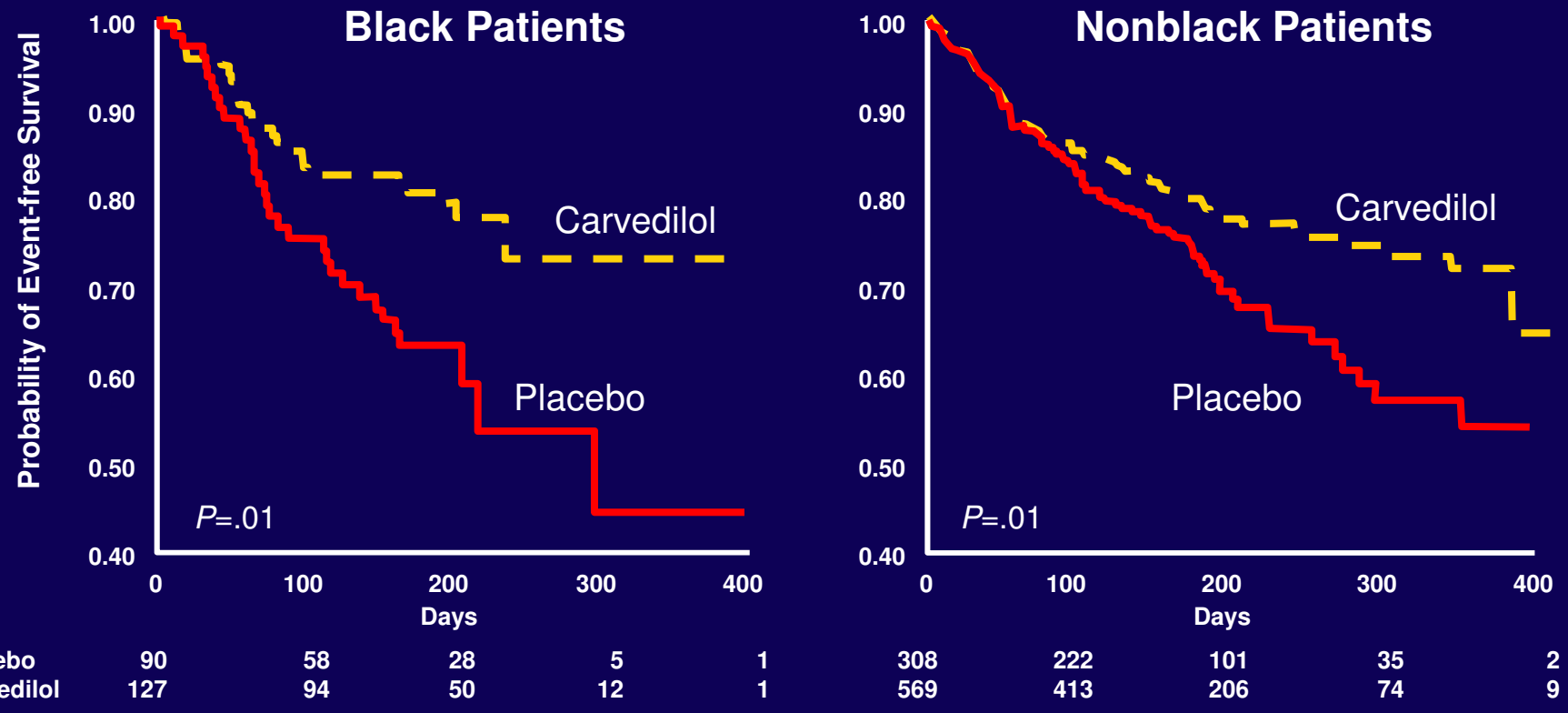
The Beta-Blocker Evaluation of Survival Trial Investigators. *N Engl J Med*. 2001;344:1659–1667.

Effect of Bucindolol on Mortality by Race



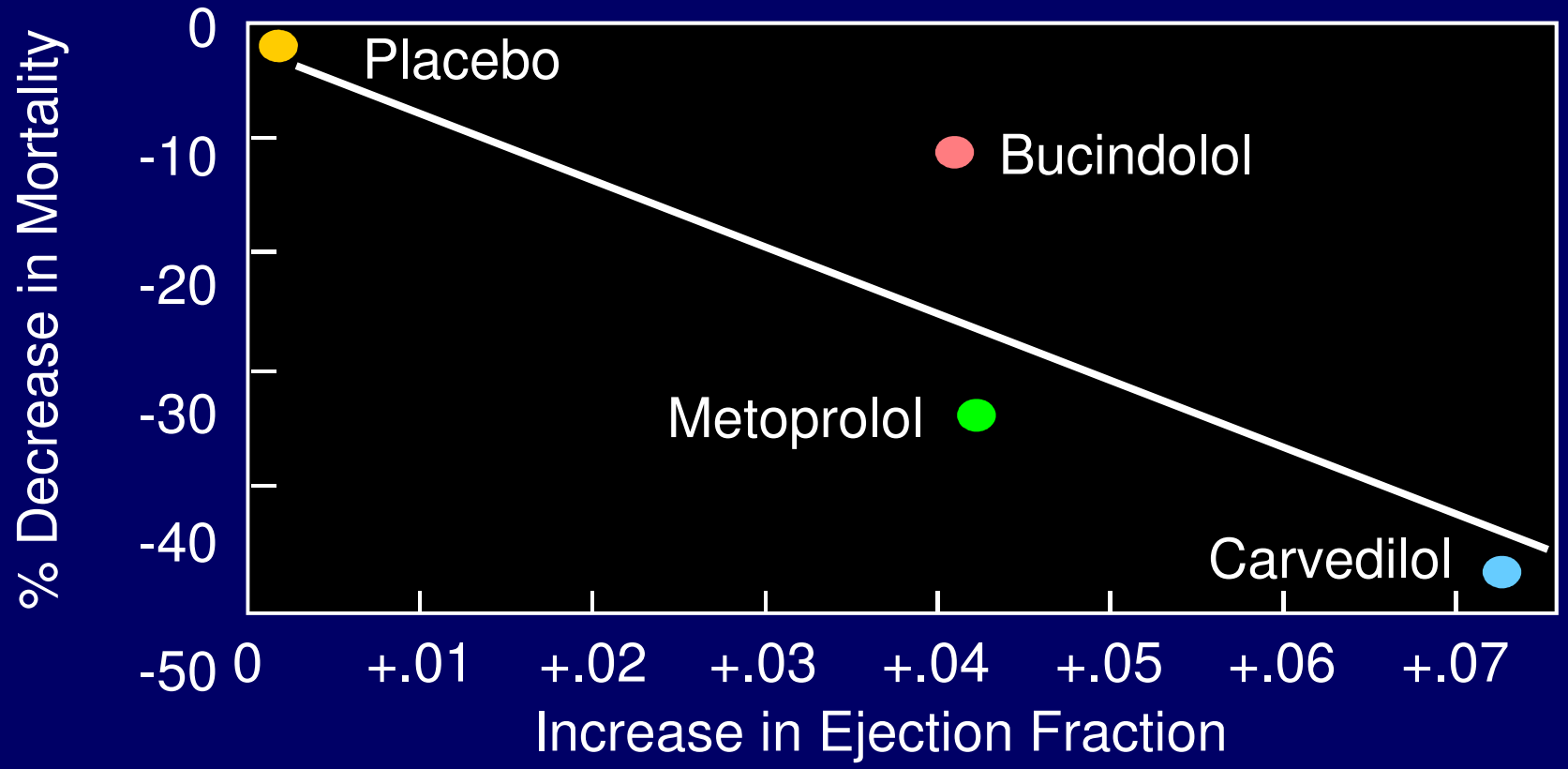
Domanski M., Presentation at ACC 2000.

US Carvedilol HF Trials: Effect of Race on Death or Hospitalization for Any Cause



Yancy CW et al. *N Engl J Med.* 2001;344:1358–1365.

Effects of Beta Blocker Trials on Mortality and Ejection Fraction

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