Prophylaxis for patients who have experience a myocardial infarction

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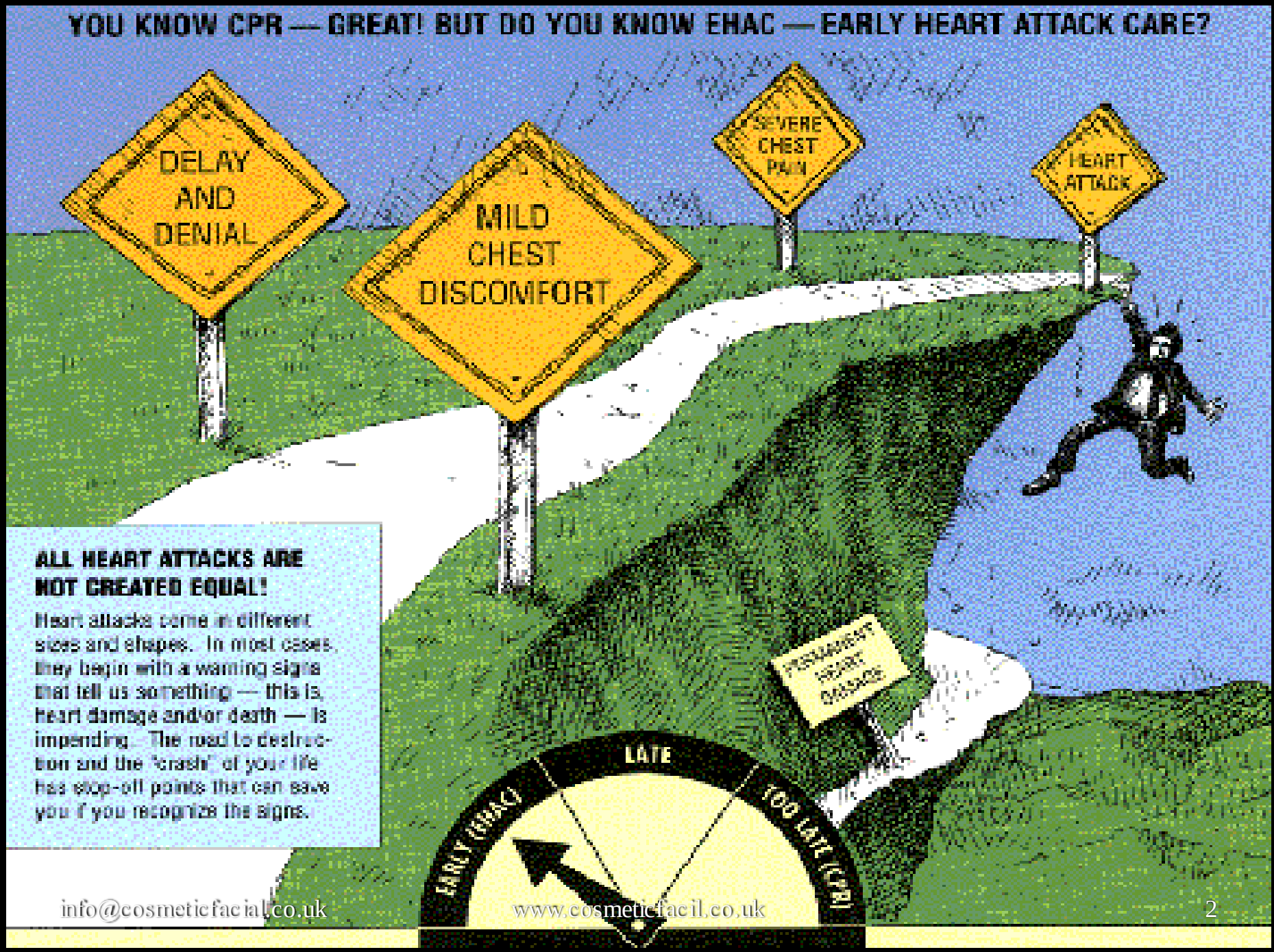

YOU KNOW CPR — GREAT! BUT DO YOU KNOW EHAC — EARLY HEART ATTACK CARE?
DELAY AND DENIAL
MILD CHEST DISCOMFORT
SEVERE CHEST PAIN
HEART ATTACK
ALL HEART ATTACKS ARE NOT CREATED EQUAL!
Heart attacks come in different sizes and shapes. In most cases, they begin with a warning signs that tell us something — this is, heart damage and/or death — is impending. The road to destruction and the "crash" of your life has stop-off points that can save you if you recognize the signs.
EARLY (EHAC)
LATE
TOO LATE (CPR)

Aim of the guideline

- To provide evidence-base recommendation to guide health care professionals in the appropriate primary care management of secondary prophylaxis for patient who have previously experience a myocardial infarction.
- Decision to adopt any particular recommendation must be made by the practitioner in the light of circumstances presented by individual patients and available resources.

Scope

- The scope of this first edition of the guideline is necessarily limited to address key areas of current uncertainty.
- Given the range of treatments available, it is increasingly important to examine the value of each and the extend to which treatments might be complementary. Thus the aim of the guideline is to provide evidence-based guidance on the value of different treatments options and their prioritisation.

The objective

- To examine and present the evidence concerning the appropriate sequencing of drugs and other intervention for secondary prophylaxis in patients with a prior MI
- And to identify whether this differs according to prognostic risk factor (principally heart failure).

categories of evidence

- Ia: evidence from meta-analysis of randomised controlled trials.
- Ib: evidence from at least one randomised controlled trial.
- IIa: evidence from at least one control study without randomisation
- IIb: evidence from at least one other type of quasi-experimental study
- IIIa: evidence from non-experimental descriptive studies, such as comparative studies, correlation and case control studies
- IV: evidence from expert committee report or opinions and/or clinical experience of respected authorities

Strength of recommendation

- A directly based on category I evidence
- B directly based on category II evidence or extrapolated recommendation from category I evidence
- C directly based on category III evidence or extrapolated recommendation from category I or II evidence
- D directly based on category IV evidence or extrapolated from category I, II,III evidence

Statins

- Based on data from randomised controlled trials in 1000 patients who have experience an MI, treatment with statins for a year will avoid about 4 death, six non-fatal MIs and 2 stroks. These benefits appear similar regardless of intial cholesterol level (Ia)
- Most of evidence comes from trials of pravastatin and simvastatin (Ib).
- Most trials started statins 12 weeks after mycardial infarction (Ia).
- The effectiveness of statin in patients who develop heart failure in addition to MI has not been adequetly assessed (Ia)
- None of the studies considered included patients with an initial cholestrol < 4 mmol/l (Ia).

Beta-blocker for unselected patient

- In 1000 unselected patients who have experienced prior MI, trearment with a beta-blocker for a year will avoid about 13 deaths 8 non-fatal MIs (Ia)
- Potential benefits from beta-blockers may be achieved through early initiation of therapy. However, these will continue to accrue over long term use (Ia).
- In 1000 patients treated for a year, in about twelve of those who discontinue therapy, the discontinuation is attributable to the drug(1a)
- Beta-blockers with intrinsic sympathomimetic activity are associated with a near significant reduction in therapeutic effect compared with agents without this characteristic (Ia)
- Most evidence for long beta-blocker use comes from trial propranolol, timolol and metoprolol

•ACE inhibitors in unselected patients

- ACE inhibitors are associated with a small reduction in short term use immediately after acute MI. in 1000 patient who have experience MI, treatment with an ACE inhibitor for a year will avoid about two death (Ia).
- In longer term use in patient at raised cardiovascular risk, ACE inhibitors are associated with a moderate reduction in mortality. If 1000 patients are treated for one year 4 deaths will be avoided (Ib).

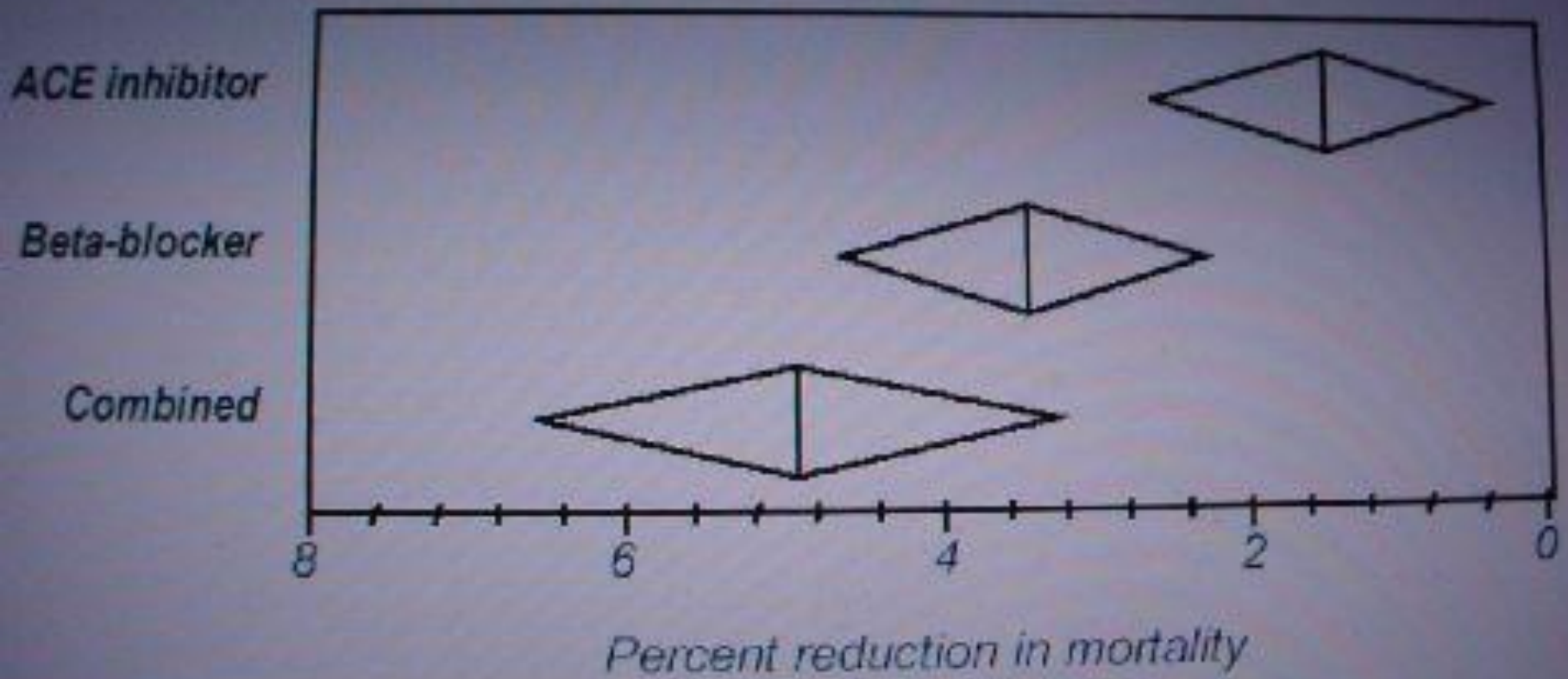
ACE inhibitors in selected patients

- Long term trearment with ACE inhibitors is associated with a substantial reduction in all causes mortality in selected patients with sign of heart failure who have recently experience an MI. treating 1000 patients with heart failure with ACE inhibitors for a year, commencing soon after an index MI, will avoid 18 deaths (Ia).
- ACE inhibitors may also reduce the incidence of non-fatal MI (Ia).
- The tolerability of ACE inhibitors in the trials was very similar to that achieved with placebo (Ia).

ACE inhibitors and beta-blockers

- Beta-blockers are associated with substantial reduction in all cause mortality in patients with symptoms of heart failure being treated with an ACE inhibitors, who may or may not have experience an MI. Treating 1000 patients with hear failure for a year with beta-blockers will avoid 35 deaths (Ia).

Figure 10: Annual reduction in the rate of death in patients with heart failure treated with an ACE inhibitor, a beta-blocker, or combination



Spironolactone in patients with sever hear failure

- Spirinolactone is associated with a decrease in all cause mortality among patients with moderate to sever heart failure treated optimally with ACE inhibitors (Ib).

Antiplatlet therapy with aspirin or alternative agents in patients with prior MI

- Antiplatlet therapy is associated with a reduction in all cause mortality and non-fatal MI in patients who experience a previouse MI (Ia).
- There is no evidence that any alternative antiplatlet agent is more effective than aspirin in this patient group; the majority of evidence comes from trials of aspirin (Ia).
- There is some evidence from subgroup analysis of major trials that the benefits of aspirin and ACE inhibitors are not completely additive in patient with heart failure (Ia).

Insulin glucose infusion followed by subcutaneous insulin in patients with diabetes with prior MI

- There is evidence that rigorous control of diabetes post myocardial infarction lowers mortality (Ib).
- Insulin-glucose infusion for at least 24 hours followed by subcutaneous insulin 4times a day for at least 3 months.

Calcium channel blockers (patient with prior MI)

- Calcium channel blockers are not associated with a reduction in mortality in patients with MI, with the exception of verapamil. However, even for verapamil the observe effect may simply be due to the play of chance (Ia).
- Several calcium channel blockers are associated with a reduction in non-fatal MI,though this effect is hard to interpret in the absence of an effect upon mortality.

Calcium channel blockers in patients with heart failure

- Calcium channel blockers do not lead to a statistically significant reduction in mortality in trials in patients with hear failure. Further data are require to provide greater certainty on the effect of calcium channel blockers in this patient group (Ia).

Potassium channel activators and nitrates in patients with prior MI

- There is no evidence to support the use of nicorandil in patients with prior MI, to prevent mortality or major morbidity (Ib).
- Two very large trails post MI found no evidence for the routine use of nitrate in patients who have experience an MI if the aim is to prevent mortality or major morbidity (Ib).

'Shall I Read That back to you Sir? Help! Help!
Help! I'm having a heart Attack! Help!

Cardiac rehabilitation

- There is a good evidence that cardiac rehabilitation that include an exercise component is associated with a reduction in mortality and morbidity in patient post myocardial infarction. If 1000 patients were treated with cardiac rehabilitation commencing soon after MI and followed up between 3 months and 5 years, 24 deaths will be avoided (Ia).

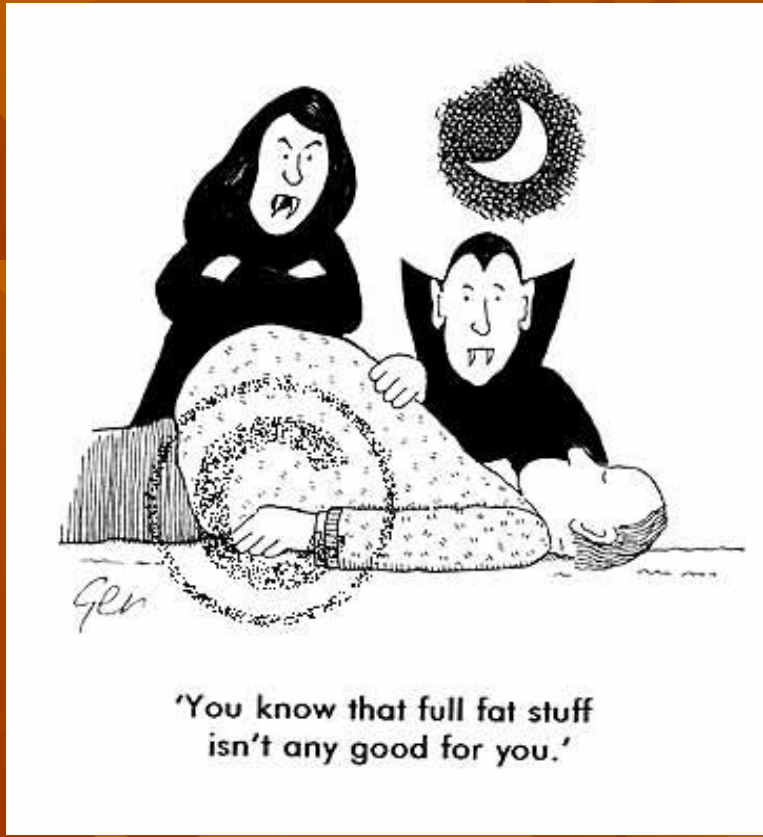
Cardiac rehabilitation

- The importance of different component of cardiac rehabilitation is poorly understood, although the trials included in the overview provided consistent result (Ia).

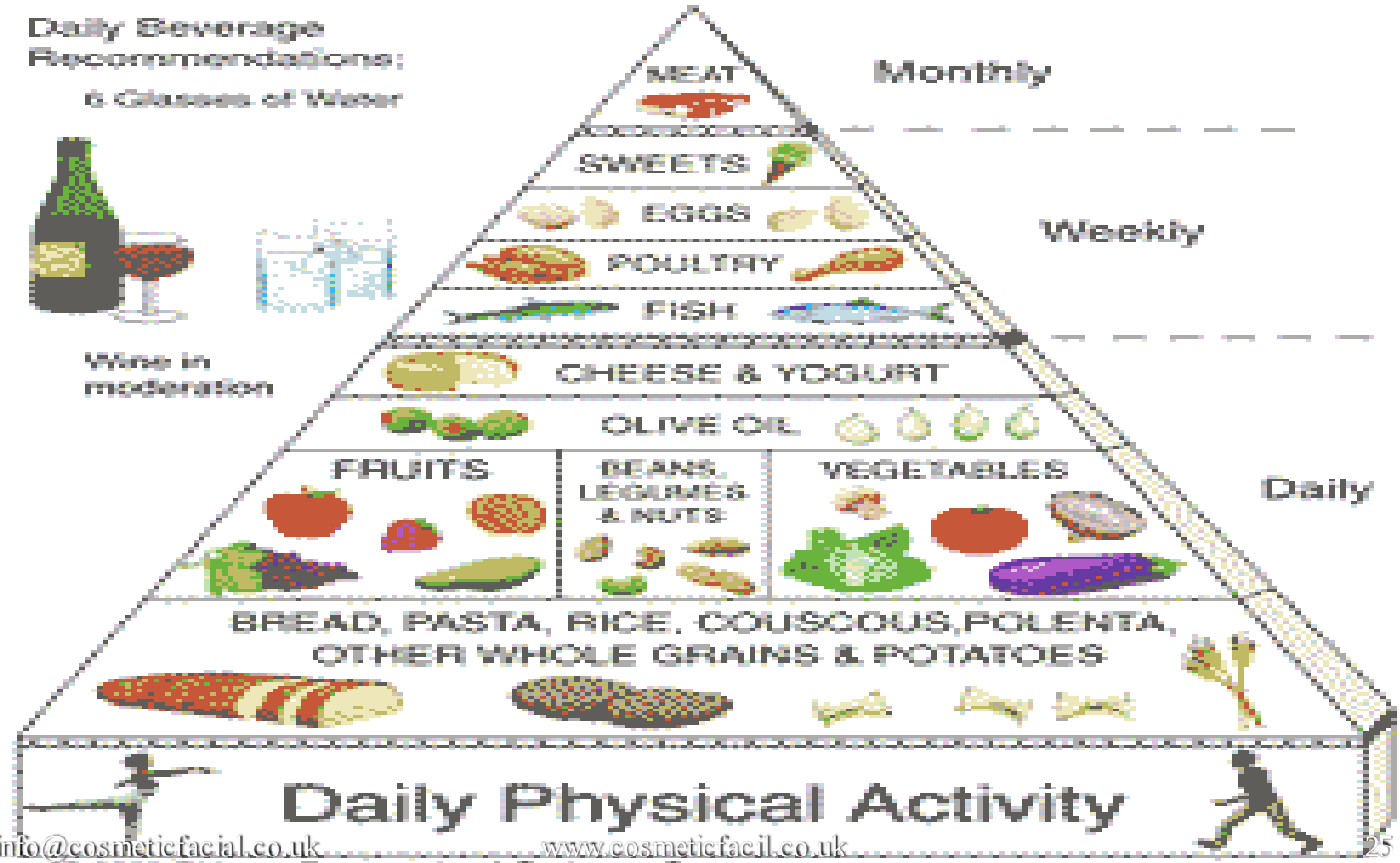

Europress
HEART ATTACK
From the award winning TV show

Mediterranean diet

- Dietary changes in line with a mediterranean type diet (in particular the avoidance of meat and dairy product and an increase in the consumption of fatty fish) appear to reduce mortality. implementing dietary advice on mediterranean diet for 1000 people for one year would lead to the avoidance of 18 deaths (Ia).



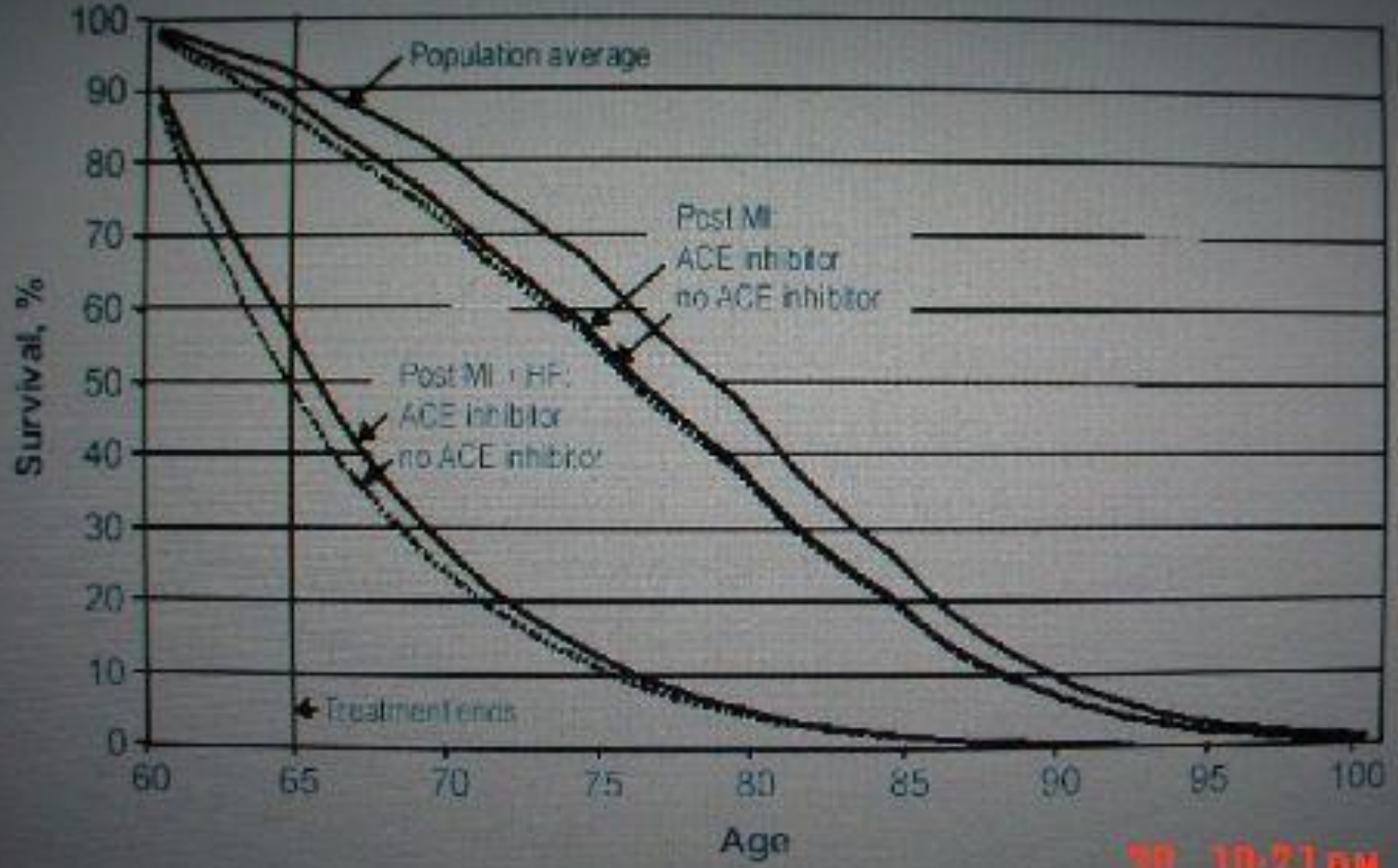
The Traditional Healthy Mediterranean Diet Pyramid



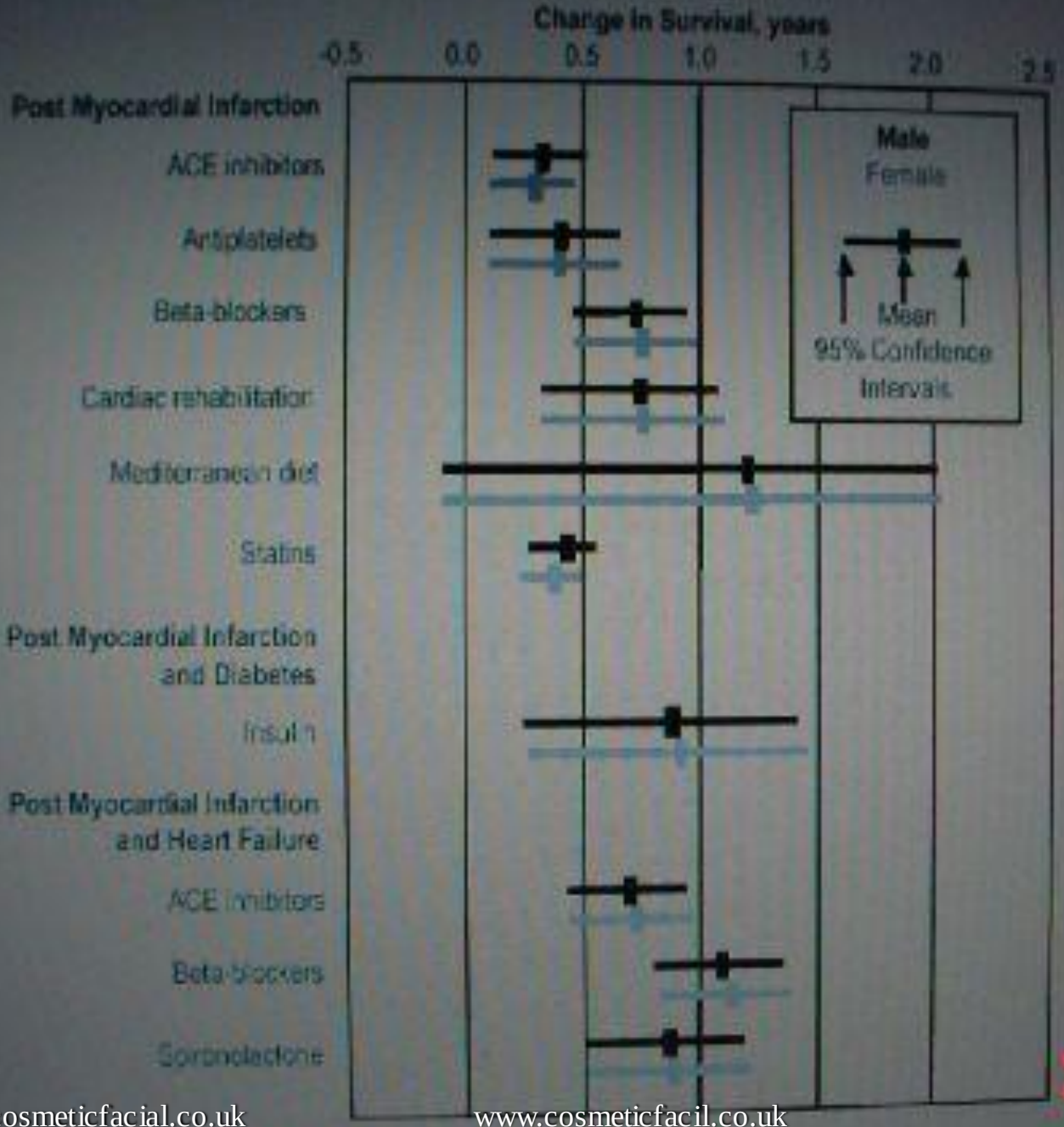
The modelling approach

- In patients with previous myocardial infarction, beta-blockers and aspirin are effective. Statins or ACE inhibitors when used in addition to these treatment are also effective. (I)
- In patients with previous myocardial infarction and heart failure ACE inhibitors are effective. In addition, spirinolactone (in moderate or sever patients) or a beta-blocker are also effective. (I)
- All available treatment are estimated to be cost-effective. (III)

Figure 20: Survival curves extrapolated from trials of patients receiving an ACE inhibitor or placebo
Curves shown are for male patients aged 60 at the start of treatment

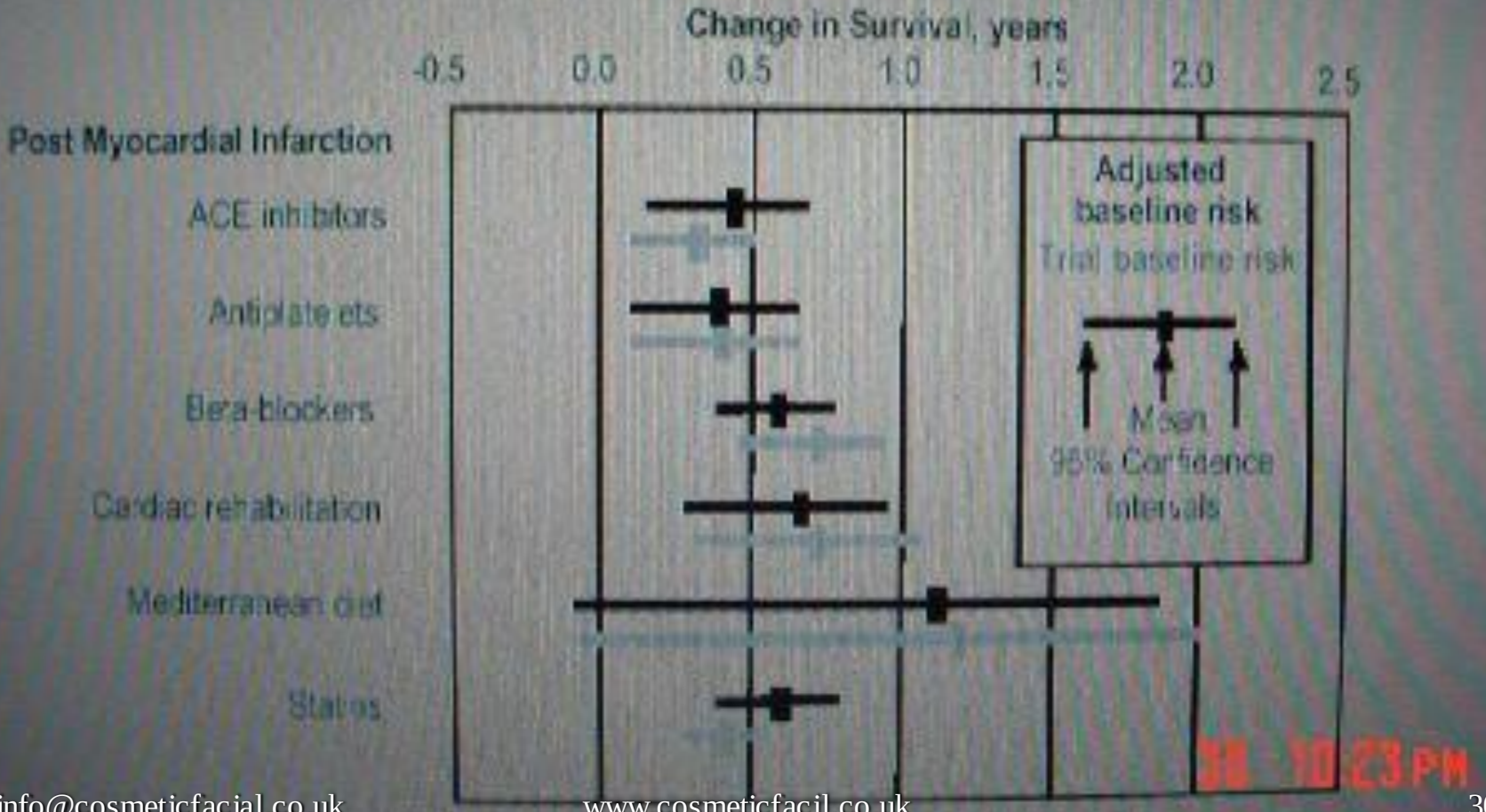


...he gain in survival is the area between the treatment and control survival curves. It is notable that


Change in Survival, years
-0.5
0.0
0.5
1.0
1.5
2.0
2.5
Post Myocardial Infarction
ACE inhibitors
Antiplatelets
Beta-blockers
Cardiac rehabilitation
Mediterranean diet
Statins
Post Myocardial Infarction and Diabetes
Insulin
Post Myocardial Infarction and Heart Failure
ACE inhibitors
Beta-blockers
Spironolactone
Male
Female
Mean
95% Confidence Intervals


10
20
50
100
200
500
1,000
2,000
5,000
10,000
20,000
Post Myocardial Infarction
ACE Inhibitors (Ramipril, 5mg bd)
Antiplatelets (Aspirin, 75mg od)
Beta-blockers (Propranolol, 80mg tds)
(Metoprolol, 100mg bd)
Cardiac Rehabilitation
Statins (Pravastatin, 40mg od)
(Simvastatin 20-40mg od)
Post Myocardial Infarction and Heart Failure
ACE Inhibitors (Captopril, 25-50mg tds)
(Ramipril 2.5-5mg bd)
Beta-blockers (Propranolol, 40mg tds)
(Bisoprolol, 5-10mg od)

Figure 23: Estimated survival gains and 95% confidence intervals assuming common underlying risk for all treatments ——, *underlying risk reported in trials* ——
(common underlying risk assumes initial 5% annual all cause mortality in all patients)
Results shown are for male patients aged 65 at the start of treatment



INHERITED *Clinical Guideline* A: Summary Table

NHS

National Institute for Clinical Excellence

Prophylaxis for patients who have experienced a myocardial infarction

drug treatment, cardiac rehabilitation and dietary manipulation

Issue date: April 200[illegible] Review date: April 200[illegible]

	Drug treatment	Monitoring	Notes	Non drug treatment
PRIOR MI NO HEART FAILURE	Early initiation (in hospital) of beta-blocker + anti-platelet drug (aspirin) + ACE-inhibitor. If not initiated in hospital, Primary Care should initiate ASAP	**ACE-inhibitors**: check renal function prior to initiation & at each significant dose increase.	Continue treatment long term. Beta-blockers & ACE-inhibitors also considered for management of symptoms (e.g. in stable angina) or risk factors (e.g. hypertension).	**Rehabilitation** Patients should be offered treatment in a rehabilitation programme that has a [illegible] exercise component within it.
	Patients not taking a statin should be [illegible] & have treatment initiated 12 weeks after index MI.	**Statins**: measure initial serum cholesterol to exclude familial lipid disorders & identify levels <4mmol/l (do not need to treat). Additional measurements to assess response & inform compliance.	Calcium channel blockers, nitrates, and potassium channel activators should only be used in patients intolerant of beta-blockers & ACE-inhibitors. Verapamil or diltiazem should be considered initially. Subsequent treatment with other calcium channel blockers, nitrates or potassium channel activators is then appropriate.	Be guided by functional ability and patient preference. **Diet**
PRIOR MI WITH HEART FAILURE	Early initiation (in hospital) of an anti-platelet drug (aspirin) plus an ACE-inhibitor. If not initiated in hospital, Primary Care should initiate ASAP.	**ACE-inhibitors**: check renal function prior to initiation & at each significant dose increase.	**Particular care is required when initiating drug treatments in this group of patients.** Continue treatment long term.	Not possible to recommend specific dietary manipulation due to nature of available evidence.
	Initiate spironolactone at any point in patients with moderate or severe heart failure (NYHA 3 or 4).	Spironolactone: monitor serum potassium.	Patients are likely to continue to need symptomatic treatment with a loop diuretics. In patients with mild symptoms of heart failure (NYHA grade 1 or 2) it is unclear whether spironolactone decreases premature mortality. It may represent a reasonable choice of adjunct symptomatic therapy.	
	Initiate beta-blockers at any point. Start with low dose & slowly increase, e.g. at fortnightly intervals, over a period of up to 12 weeks.	**Beta Blockers**: [illegible] needs hospital supervision for initiation. There may be a group of patients with heart failure for whom GPs (based on their knowledge of the patient's clinical condition) feel able to initiate. Discussion at a local level may inform appropriate methods.	There is no evidence on which to recommend the use of statins. Statin use will be influenced by clinical and practical considerations, such as whether patients were treated with them prior to developing heart failure.	
PRIOR MI WITH DIABETES	There is evidence that intensive insulin therapy initiated soon after admission for acute myocardial infarction reduces mortality. To achieve the benefits demonstrated in the single trial in this area involves 4 daily insulin injections continuing for at least 3 months.			

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Which drug?
MI without heart failure

- Long term treatment firstly with a beta-blocker and an antiplatlet (aspirin), and then with a statins and an ACE inhibitors (A).
- Licence indications currently suggest a lower limit of 4.8 mmol/l or 5.5 mmol/l depending on the drug used (D).
- Beta-blockers and ACE inhibitors will also be considered for the management of symptoms or risk factors (e.g hypertension) (D).
- Calcium channel blockers, nitrates, and potassium channel activators have no effect on premature mortality making their role the management of symptoms and risk factors (A).

Continuation of treatment

- Based on the evidence from the trial, treatment should continue long term (D).
- 3 and ½ years for antiplatlet (aspirin) (D)
- 4 years for beta-blockers and ACE inhibitors (D)
- Six years for statins (D)
- In the absence of a clear reason to stop treatment, it seems reasonable to continue treatment indefinitely (D).

MI and heart failure

- Long term treatment (A)
- ACE inhibitor and then a beta-blocker (A)
- In addition antiplatlet drug (aspirin) (A)
- Spirnolactone in patients with moderate or sever hear failure (A)
- Patients are likely to need symptomatic treatment with a loop diuretic (D)
- Statins use will be influence by clinical and practical consideration (D).

Continuation of treatment

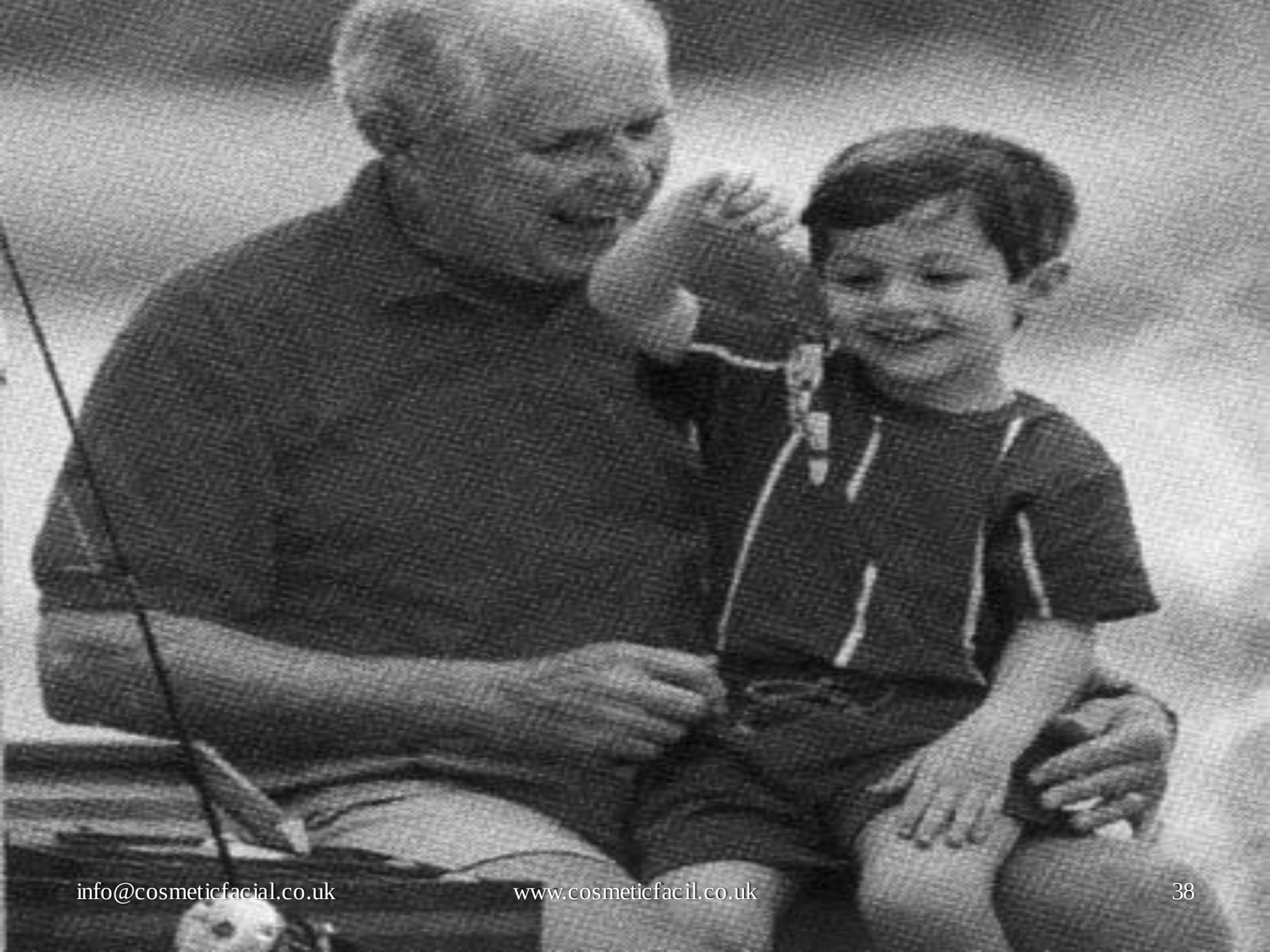
- Treatment should continue long term (D).
- 3 and half years for ACE inhibitors (D)
- 2 and half years for beta-blockers (D)
- 2 years for spirinolactone (D)
- In the absence of a clear reason to stop treatment it seems reasonable to continue treatment indefinitely (D)

Rehabilitation

- Patient should be offered enrolment in a rehabilitation programme that has a prominent exercise component in it (A).
- Functional mobility and patient preference should be considered instead of upper age limit for recruitment (D)

Diet

- Given the nature of the available evidence of the effectiveness of the dietary manipulation as a strategy for secondry prevention it is not possible to recommend specific dietary manipulation (B).



Thank you

Any feed back and comments?