

L'infarto “ST sopra” ed il suo trattamento oggi

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UO Cardiologia

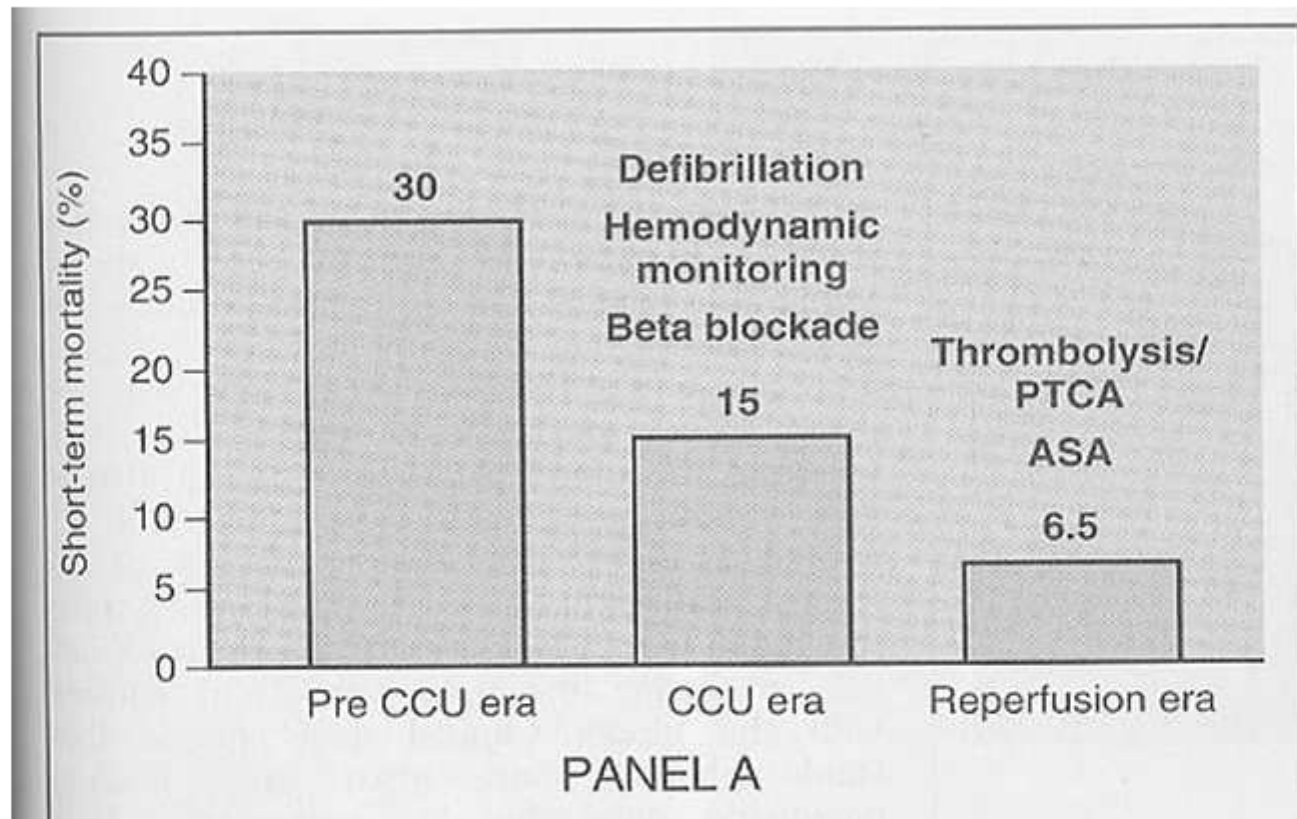
Sabato 21 gennaio 2017

Aula Magna Nuovo Arcispedale S. Anna Cona Ferrara

L'infarto “ST sopra” ed il suo trattamento oggi

- **L'infarto oggi**
 - *I numeri dell'infarto*
- **Il trattamento della fase acuta**
 - *La riperfusione*
 - *Accenni di terapia farmacologica, controllo glicemico, trattamento della coronaropatia multivasale*

I numeri dell'infarto



Braunwald E - 1997

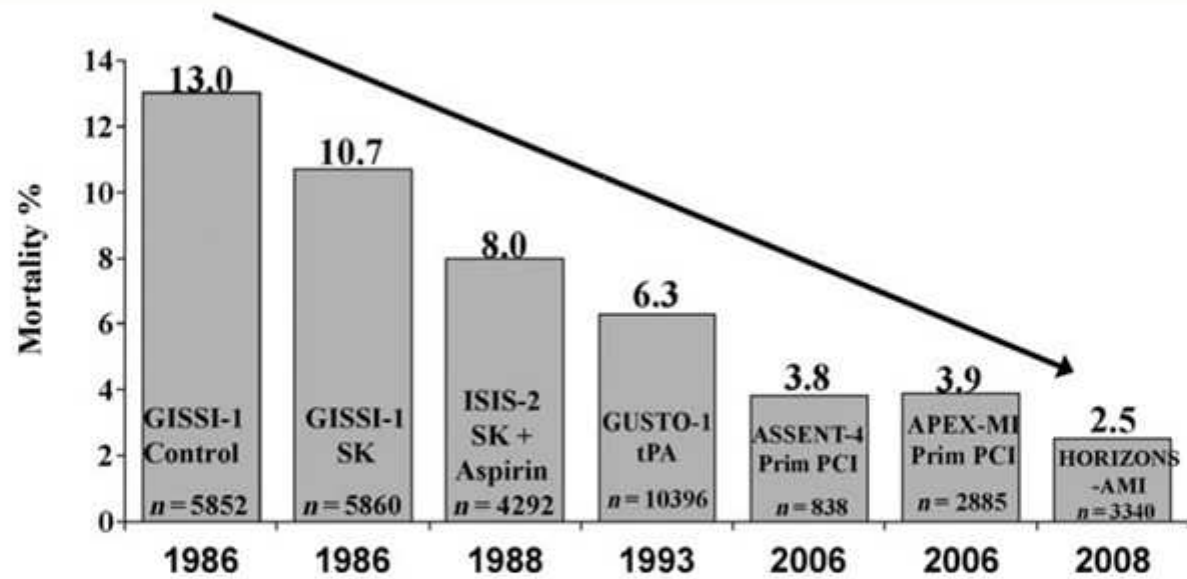


Figure 1 Early mortality rates in major randomized STEMI trials: 1986–2008.

Van de Werf F: The history of coronary reperfusion. Eur Heart J 2014; 35: 2510-15.



European Heart Journal (2016) **37**, 3232–3245
doi:10.1093/eurheartj/ehw334

REVIEW

Cardiovascular disease in Europe: epidemiological update 2016

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Table 7 Case-fatality rates after AMI and stroke, latest year, by country

Country	Year	Case fatality after acute myocardial infarction		Case fatality after ischaemic stroke	
		Admission based	Patient based	Admission based	Patient based
Austria	2013	10.0	—	6.4	—
Belgium ^a	2013	7.3	—	9.3	—
Czech Republic	2013	6.7	10.5	9.6	13.0
Denmark ^a	2013	5.7	8.3	9.1	10.2
Estonia	2013	11.5	13.1	13.0	13.2
Finland	2013	6.5	8.5	5.1	6.8
France	2013	7.2	—	7.9	—
Germany	2013	8.7	—	6.4	—
Iceland	2013	6.9	—	8.0	—
Ireland ^a	2013	6.4	—	9.7	—
Israel ^a	2013	6.7	8.8	6.0	8.1
Italy	2013	5.5	7.5	6.2	9.0
Latvia	2013	15.4	19.1	18.4	27.0
Luxembourg ^a	2012	7.0	10.5	9.1	11.1
The Netherlands ^a	2011	7.6	7.7	7.1	9.6
Norway	2013	6.7	7.6	5.4	8.4
Poland	2013	4.7	8.2	—	—
Portugal	2013	9.4	10.4	10.2	10.8
Slovak Republic ^a	2012	7.2	—	10.8	—
Slovenia	2013	5.2	9.0	13.2	14.9
Spain	2013	7.8	8.2	9.7	9.9
Sweden ^a	2013	4.5	8.3	6.4	9.6
Switzerland	2013	7.7	8.9	6.9	8.2
UK ^a	2013	7.6	9.1	9.2	10.6

Case-fatality rate measures the percentage of people aged 45 and over who die within 30 days following admission to hospital for a specific acute condition.

Total rates have been age–sex standardized to the 2010 OECD population (45+).

Admission-based rates refer to death occurring in the same hospital as the initial admission.

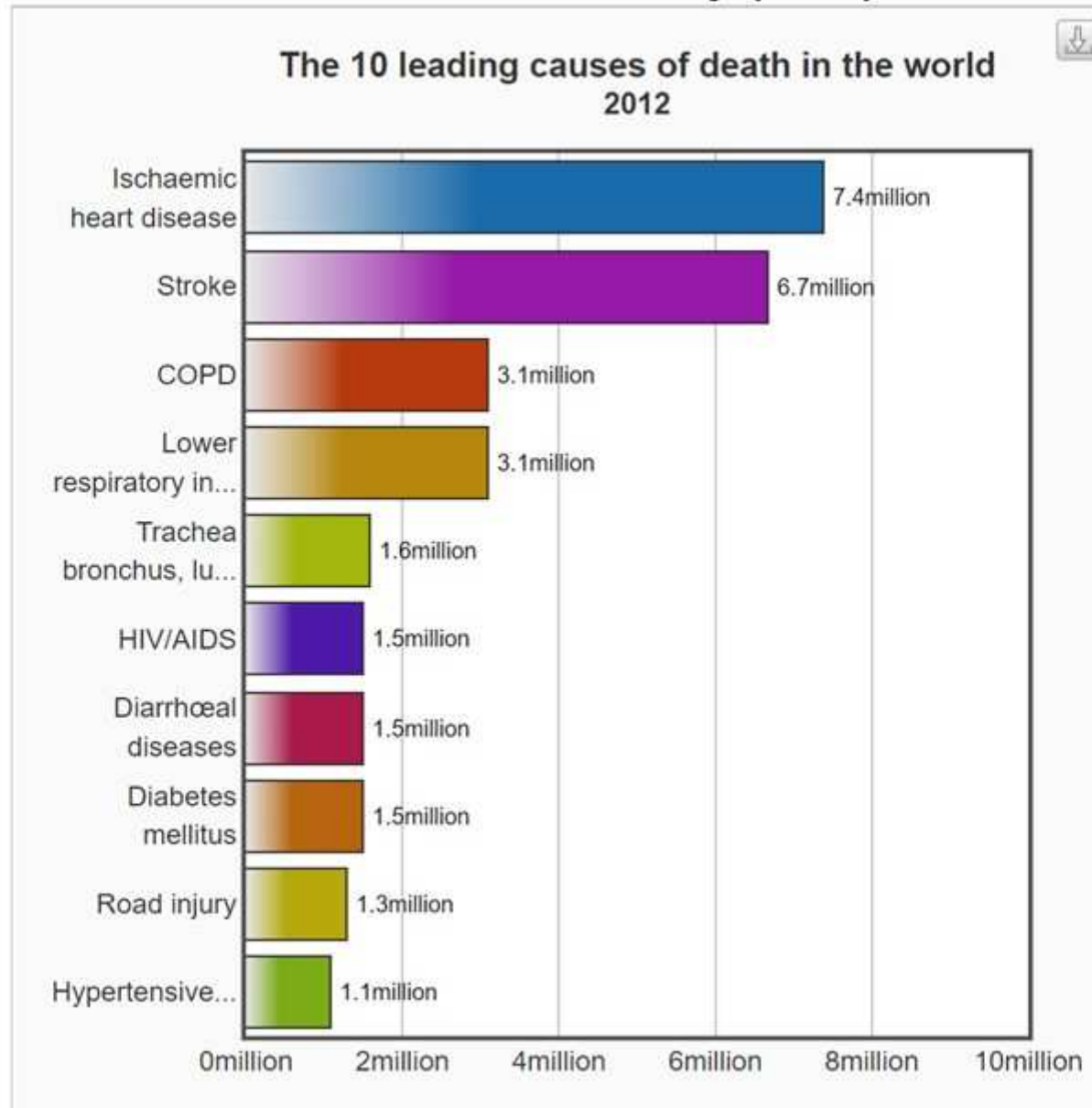
Patient-based rates refer to death occurring in the same hospital as the initial admission, a different hospital, or out of hospital.

Three-year average for Iceland and Luxembourg.

^aAdmissions resulting in a transfer are included.

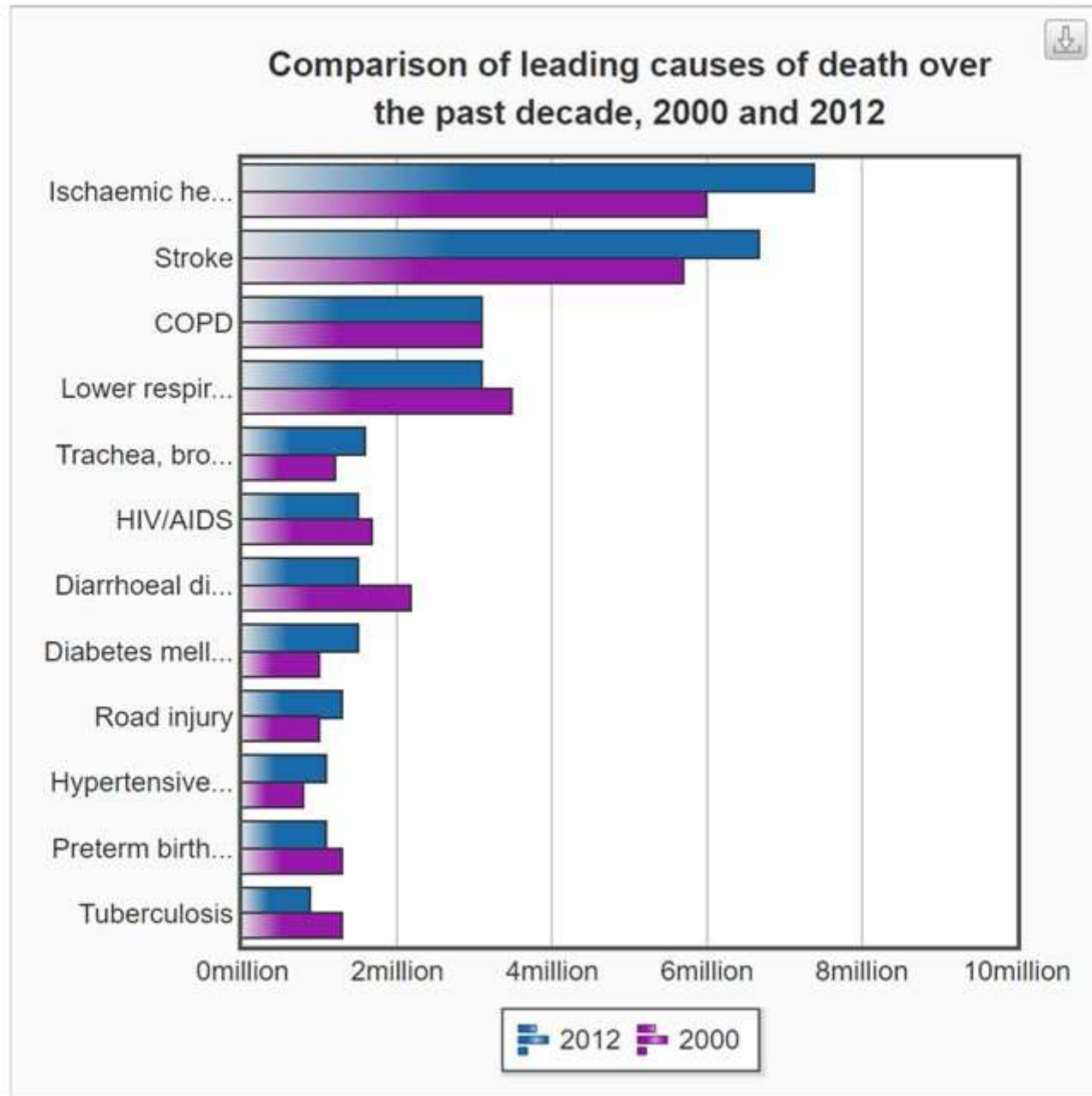
Source: OECD Health Statistics 2015, <http://dx.doi.org/10.1787/health-data-en>.

Global Health Observatory (GHO) Data



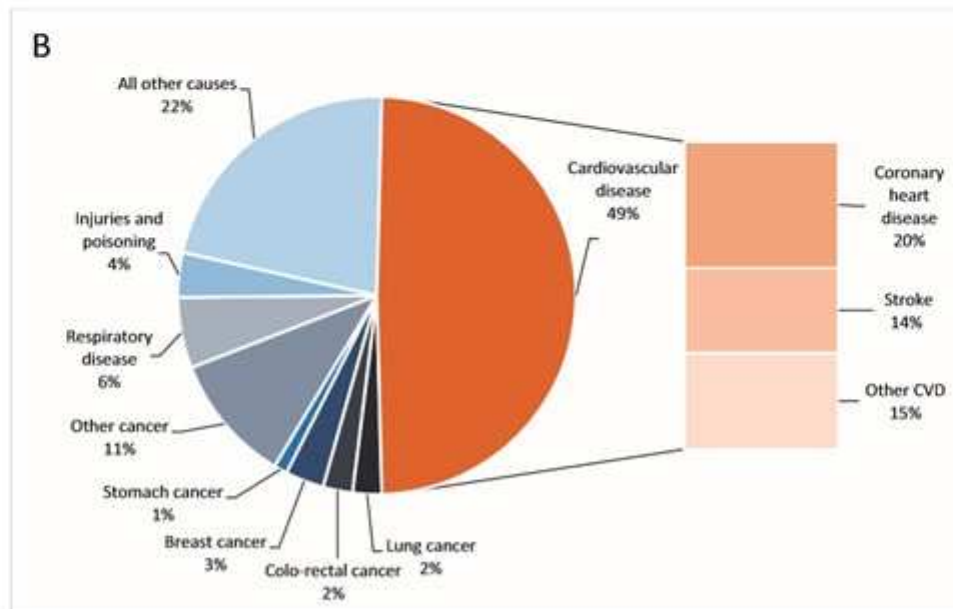
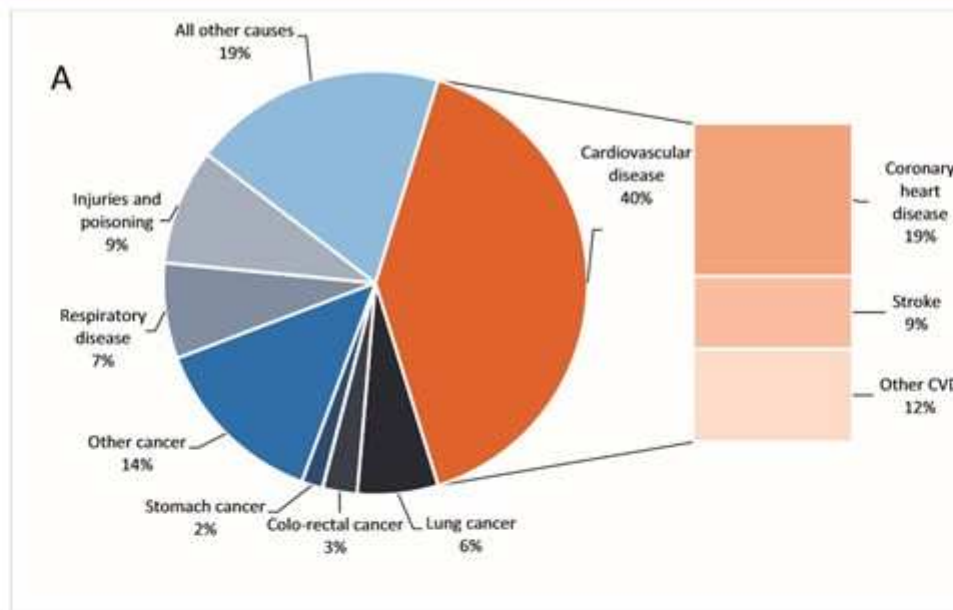
WHO Mortality Database 2016

Global Health Observatory (GHO) Data



Proportion of all deaths due to major causes in Europe

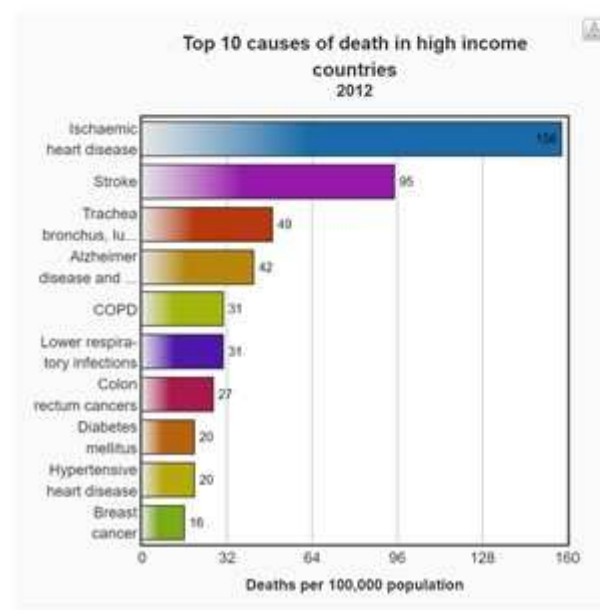
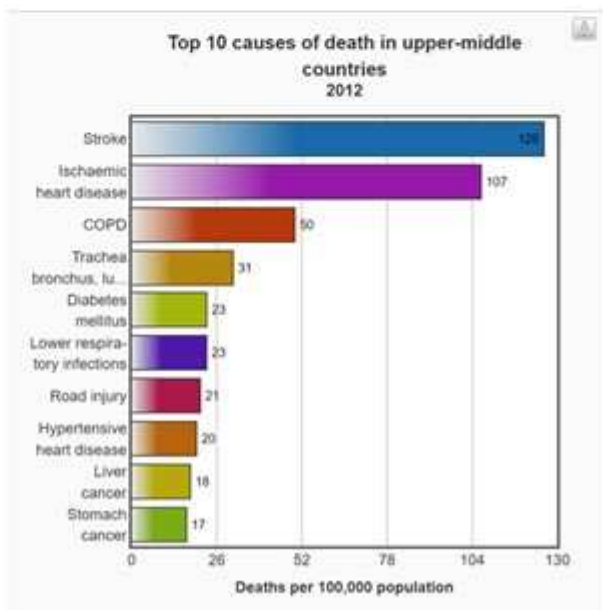
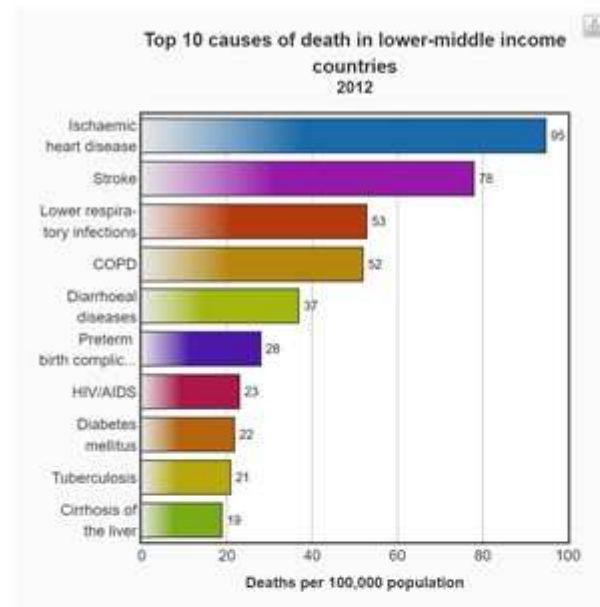
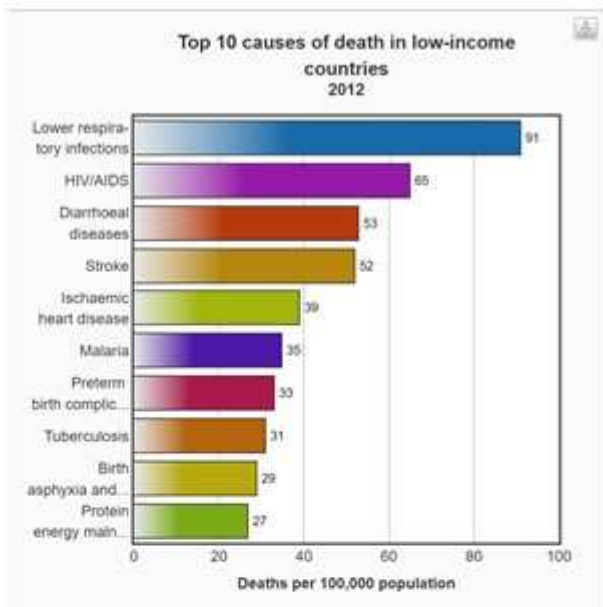
WHO Mortality Database (2015 update)



Note: no data available for Andorra.
Source: WHO Mortality Database.

Global Health Observatory (GHO) Data

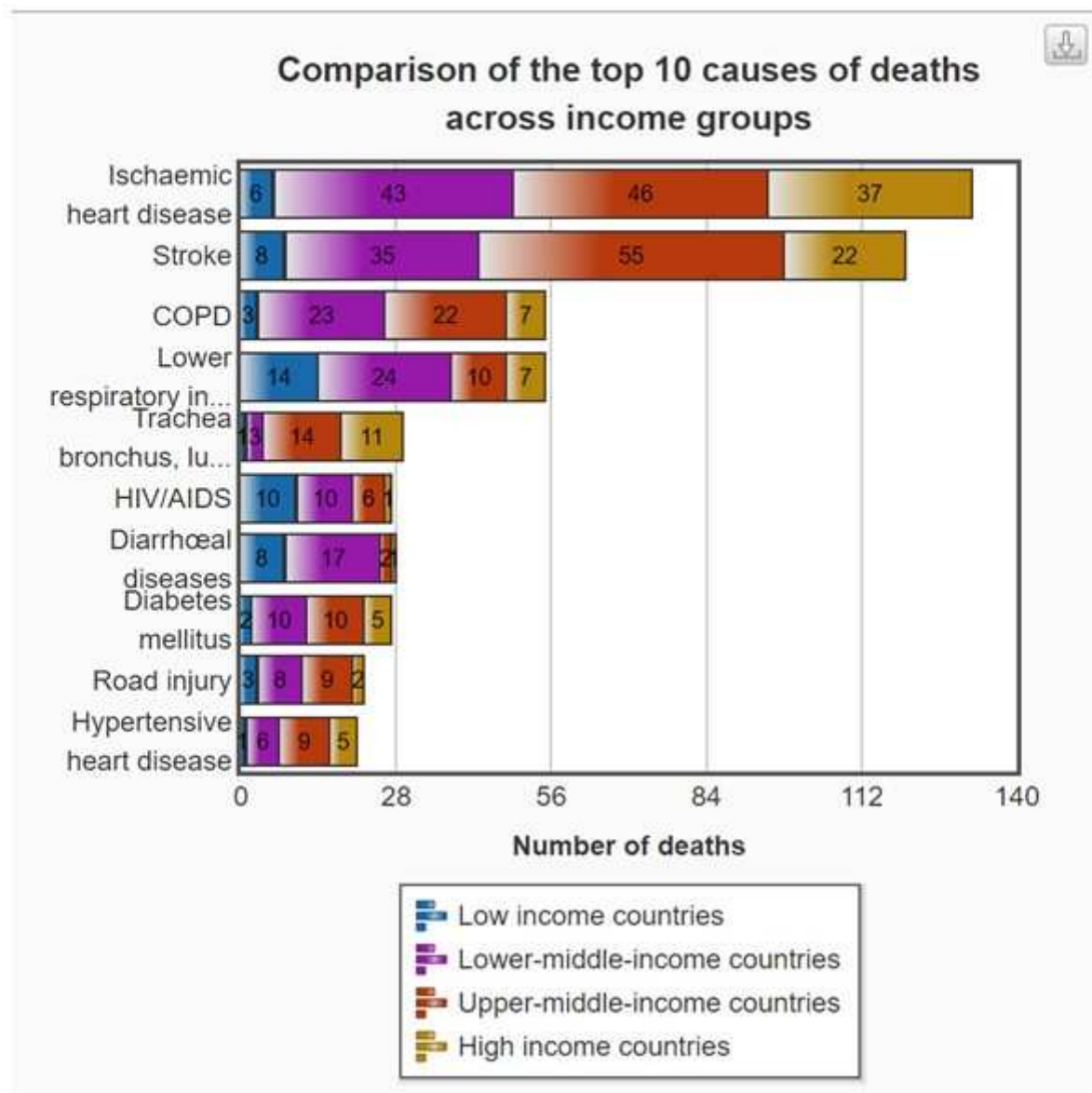
The 10 leading causes of death by country income group (2012)

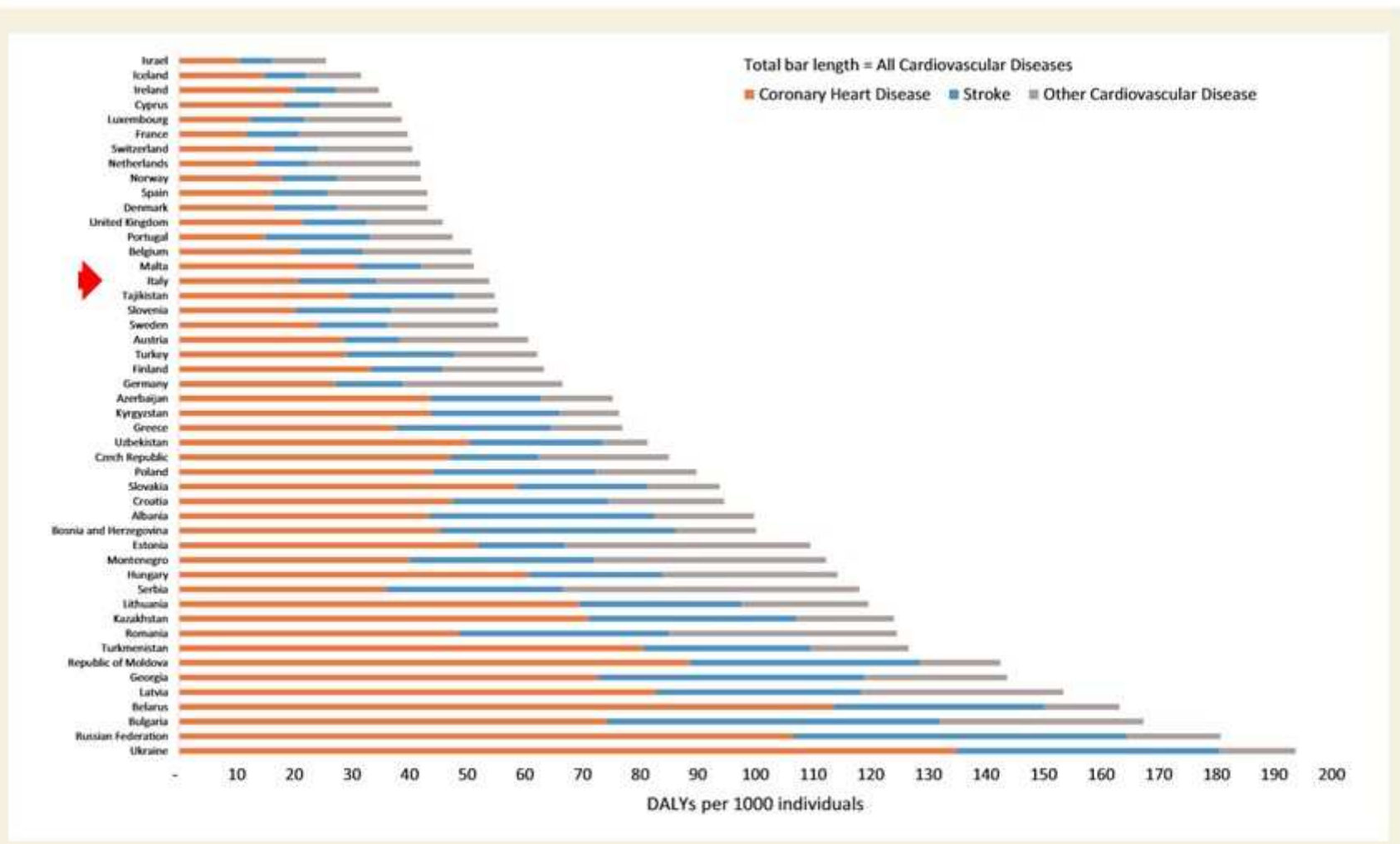


Global Health Observatory (GHO) Data

Deaths across the globe: an overview

(1000 individuals died in 2012)





AHA Statistical Update

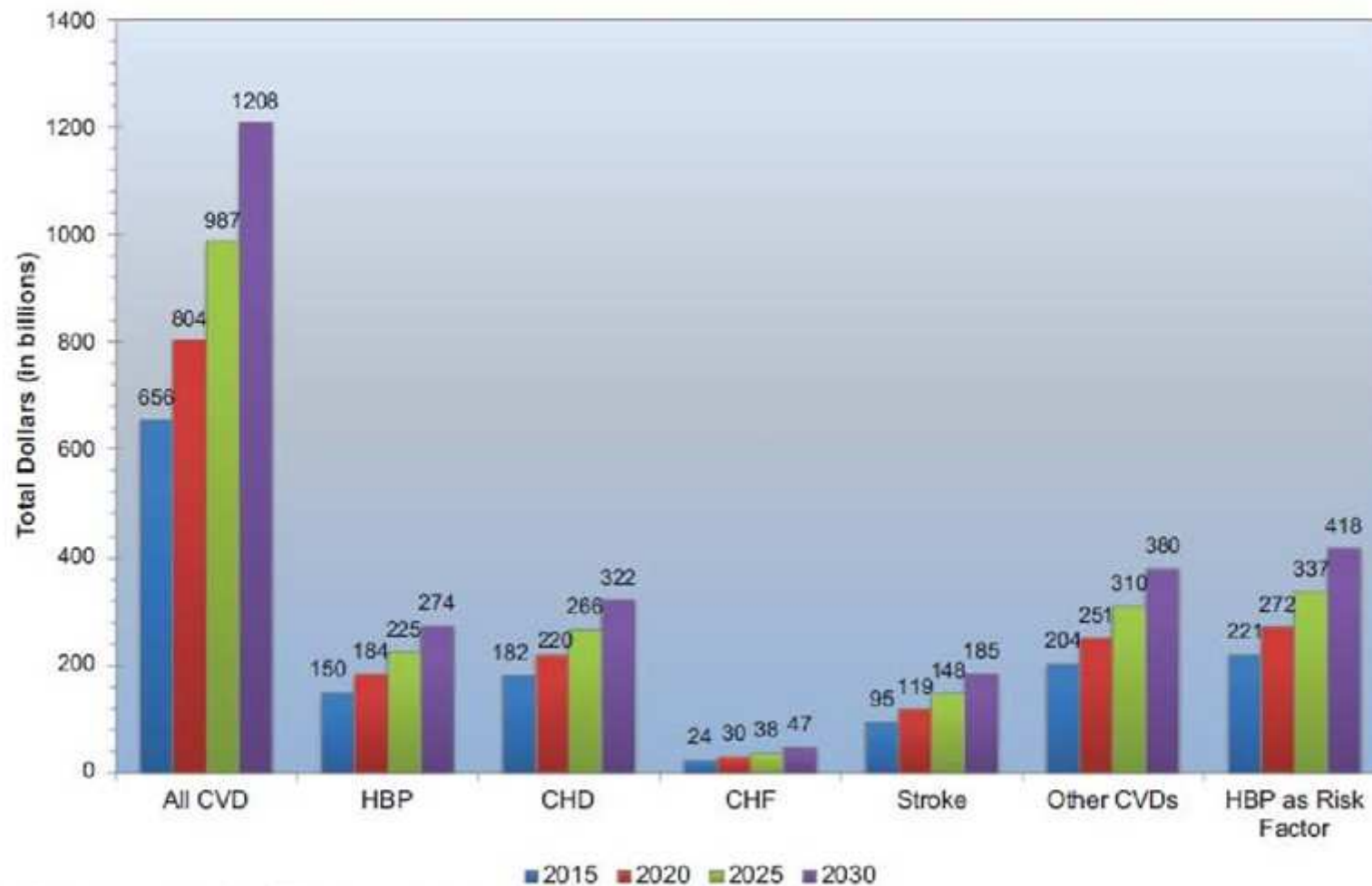
Executive Summary: Heart Disease and Stroke Statistics—2016 Update

A Report From the American Heart Association

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the American Heart Association Statistics Committee and Stroke Statistics Subcommittee

Projected Total Costs of CVD, 2015–2030 (in Billions 2012\$) in the United States



Unpublished data tabulated by AHA using methods described in *Circulation*. 2011;123:933–944.

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Mozaffarian D et al. Published online in *Circulation* Dec. 16, 2015

HEALTH POLICY STATEMENT

Our Time: A Call to Save Preventable Death From Cardiovascular Disease (Heart Disease and Stroke)

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and European Society of Cardiology (R.F., D.A.W.)*

Appendix C. Current Set of Targets

Outcome Targets	Indicator	Data Source(s)
Premature mortality from NCDs 25% Relative reduction in overall mortality from CVD, cancer, diabetes, or chronic respiratory disease	Unconditional probability of dying between ages 30–70 y from CVD, cancer, diabetes, or chronic respiratory disease	Civil registration system, with medical certification of cause of death, or survey with verbal autopsy
Exposure Targets		
Alcohol 10% Relative reduction in overall alcohol consumption (including hazardous and harmful drinking)	Total (recorded and unrecorded) alcohol per capita (≥ 15 y) consumption within a calendar year in liters of pure alcohol	Official statistics and reporting systems for production, import, export, and sales or taxation data
Fat intake 15% Relative reduction in mean proportion of total energy intake from saturated fatty acids (SFA), with aim of achieving recommended level of <10% of total energy intake	Age-standardized mean proportion of total energy intake from saturated fatty acids (SFA) in adults aged ≥ 18 y	National survey
Obesity Halt the rise in obesity prevalence	Age-standardized prevalence of obesity among adults aged ≥ 18 y	National survey (with measurement)
Physical inactivity 10% Relative reduction in prevalence of insufficient physical activity	Age-standardized prevalence of insufficient physical activity in adults aged ≥ 18 y	National survey
Raised blood pressure 25% Relative reduction in prevalence of raised blood pressure	Age-standardized prevalence of raised blood pressure among adults aged ≥ 18 y	National survey (with measurement)
Raised cholesterol 20% Relative reduction in prevalence of raised total cholesterol	Age-standardized prevalence of raised total cholesterol among adults aged ≥ 18 y	National survey (with measurement)
Salt/sodium intake 30% Relative reduction in mean population intake of salt, with aim of achieving recommended level of <5 g/d (2,000 mg of sodium)	Age-standardized mean adult (aged ≥ 18 y) population intake of salt per day	National survey (with measurement)
Tobacco 30% Relative reduction in prevalence of current tobacco smoking	Age-standardized prevalence of current tobacco smoking among persons aged ≥ 15 y	National survey
Health Systems Response Targets		
Drug therapy to prevent heart attacks and strokes 50% Of eligible people receive drug therapy to prevent heart attacks and strokes, and counseling	Drug therapy to prevent heart attacks and strokes (including glycemic control), and counseling for people aged ≥ 40 y with a 10-year cardiovascular risk $\geq 30\%$ (includes those with existing cardiovascular disease)	National survey
Essential NCD medicines and basic technologies to treat major NCDs 80% Availability of basic technologies and generic essential medicines required to treat major NCDs in both public and private facilities	Availability of basic technologies and generic essential medicines required to treat major NCDs in public and private sector facilities, including primary care facilities	Facility data

NCDs indicate noncommunicable diseases; CVD, cardiovascular disease.

Table 1. Suggested Global Targets to Address NCDs With Wide Support (See Appendix C)

Proposed Target	Best Buy	Recommendation to Member States
1 Physical inactivity: 10% Relative reduction in prevalence of insufficient physical activity	✓	Adopt
2 Raised blood pressure: 25% Relative reduction in prevalence of raised blood pressure	✓	Adopt
3 Salt/sodium intake: 30% Relative reduction in mean population intake of salt, with aim of achieving recommended level of <5 g/d (2,000 mg of sodium)	✓	Adopt
4 Tobacco: 30% Relative reduction in prevalence of current tobacco smoking	✓	Adopt

NCDs indicate noncommunicable diseases.

Major gaps in evidence

- Strategies to minimize early cardiac arrest.
- Improving patient and public awareness of STEMI symptoms.
- Optimizing clinical pathways for high-quality, homogeneous early STEMI diagnosis and management.
- Reducing or minimizing myocardial injury and left ventricular dysfunction following STEMI.
- Defining the optimal management strategy for non-culprit vessels in primary PCI patients.
- Defining the optimal long-term antithrombotic regimen in patients receiving stents and who have an indication for oral anticoagulants.
- Defining the role for pre-hospital thrombolysis in patients presenting early.

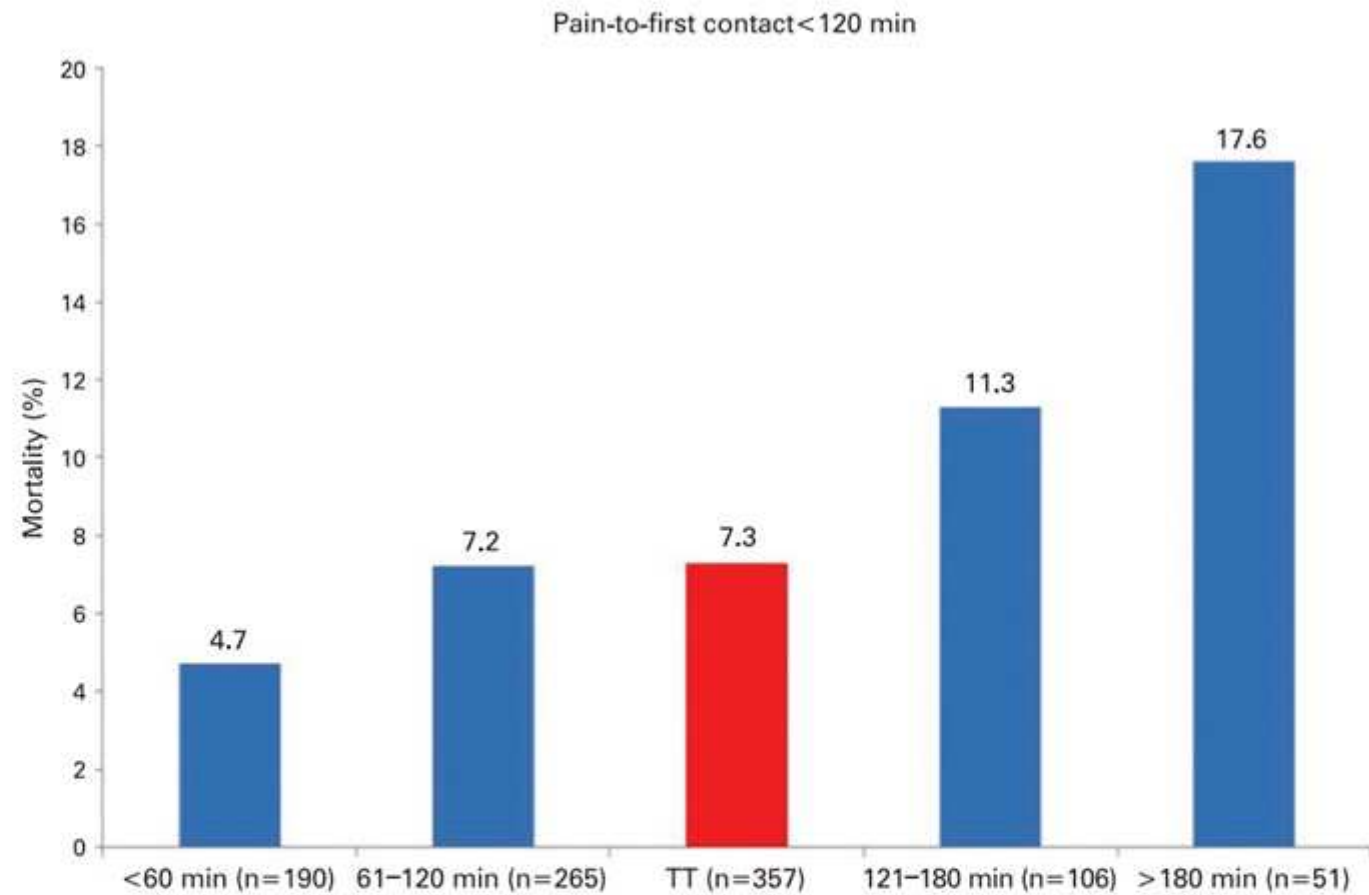
“So, today, the only realistic strategy to reduce reperfusion injury in STEMI patients is to reperfuse as early as possible. This can be achieved through early diagnosis and immediate intervention using an effective network allowing ambulance diagnosis with direct access to intervention facilities. Clearly, the implementation of these networks has resulted in remarkably good results but still to the benefit of too few patients.”

R.Ferrari et al. Can We Improve Myocardial Protection during Ischaemic Injury?
Cardiology 2016;135:14–26

Il trattamento dell'infarto

1) La riperfusione

Figure 2 In-hospital mortality rates (%) in patients with short onset of pain referred for primary percutaneous coronary intervention (pPCI) with respect to the time delay from first medical contact to first balloon inflation, in comparison with thrombolytic treatment performed if pPCI could not be offered within 90–120 min. TT, thrombolytic treatment.



The Vienna STEMI network

Kalla K, Christ G, Karnik R, et al. Implementation of guidelines improves the standard of care: the Viennese registry on reperfusion strategies in ST-elevation myocardial infarction (Vienna STEMI registry). *Circulation* 2006;113:2398–405.

Primary PCI

Recommendations	Class	Level
Indications for primary PCI		
Primary PCI is the recommended reperfusion therapy over fibrinolysis if performed by an experienced team within 120 min of FMC.	I	A
Primary PCI is indicated for patients with severe acute heart failure or cardiogenic shock, unless the expected PCI related delay is excessive and the patient presents early after symptom onset.	I	B

FMC = first medical contacts; PCI = percutaneous coronary intervention.

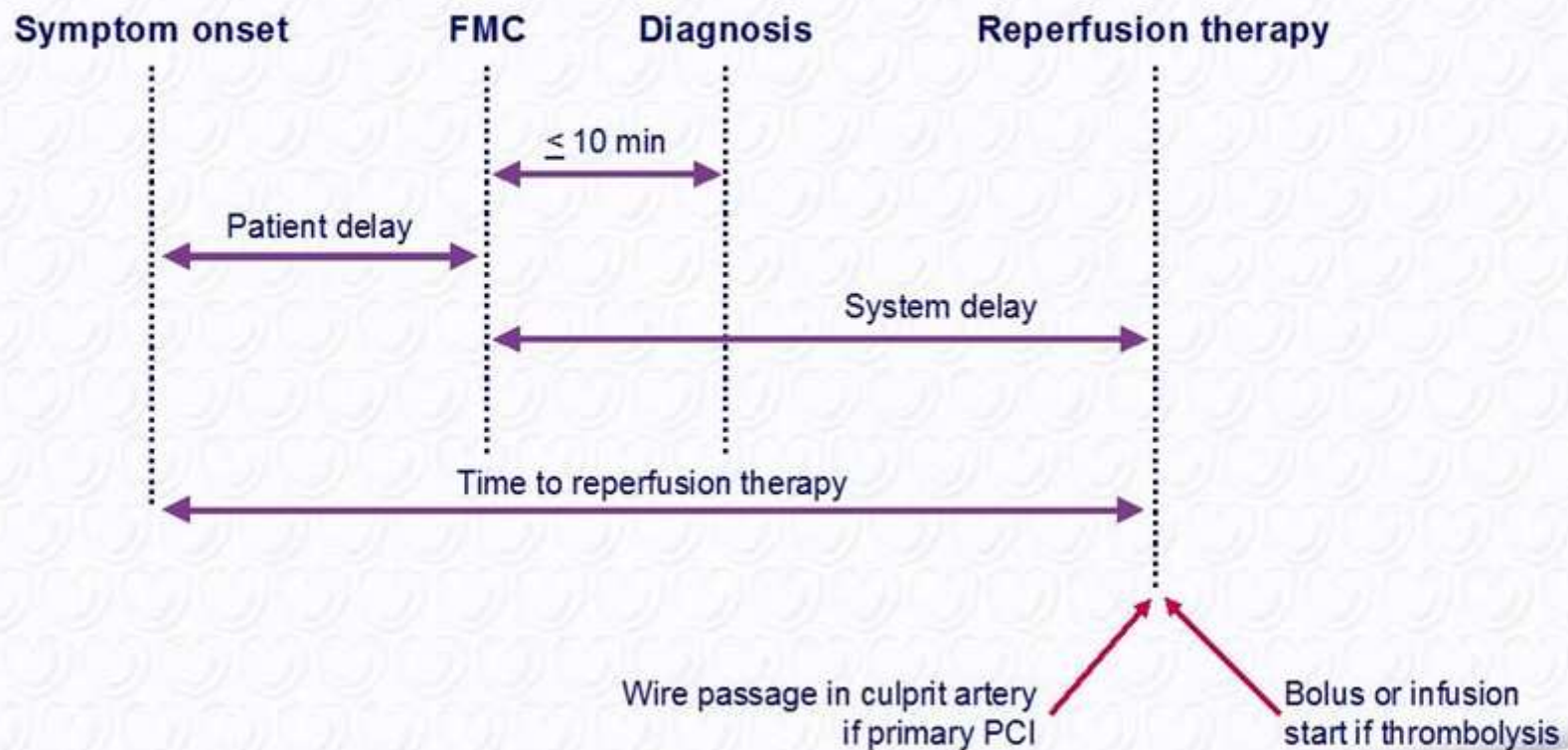
La rete

Table 1 Essential for ST-elevation myocardial infarction systems of care

Single telephone emergency number
Ambulances (vehicles, helicopters, planes), equipped with 12-lead ECGs and defibrillators, and staffed with physicians or well-trained paramedics, capable of basic and advanced life support
Occasionally automatic ECG interpretation or ECG telemetry
Direct telephone access to the cath lab
Protocols for standardized care (diagnosis, therapy, and transfer)
Cardiologist or intensive care specialist as a network leader
Involvement of healthcare authorities
Public information campaigns
Regular meetings of involved parties
Prospective registry

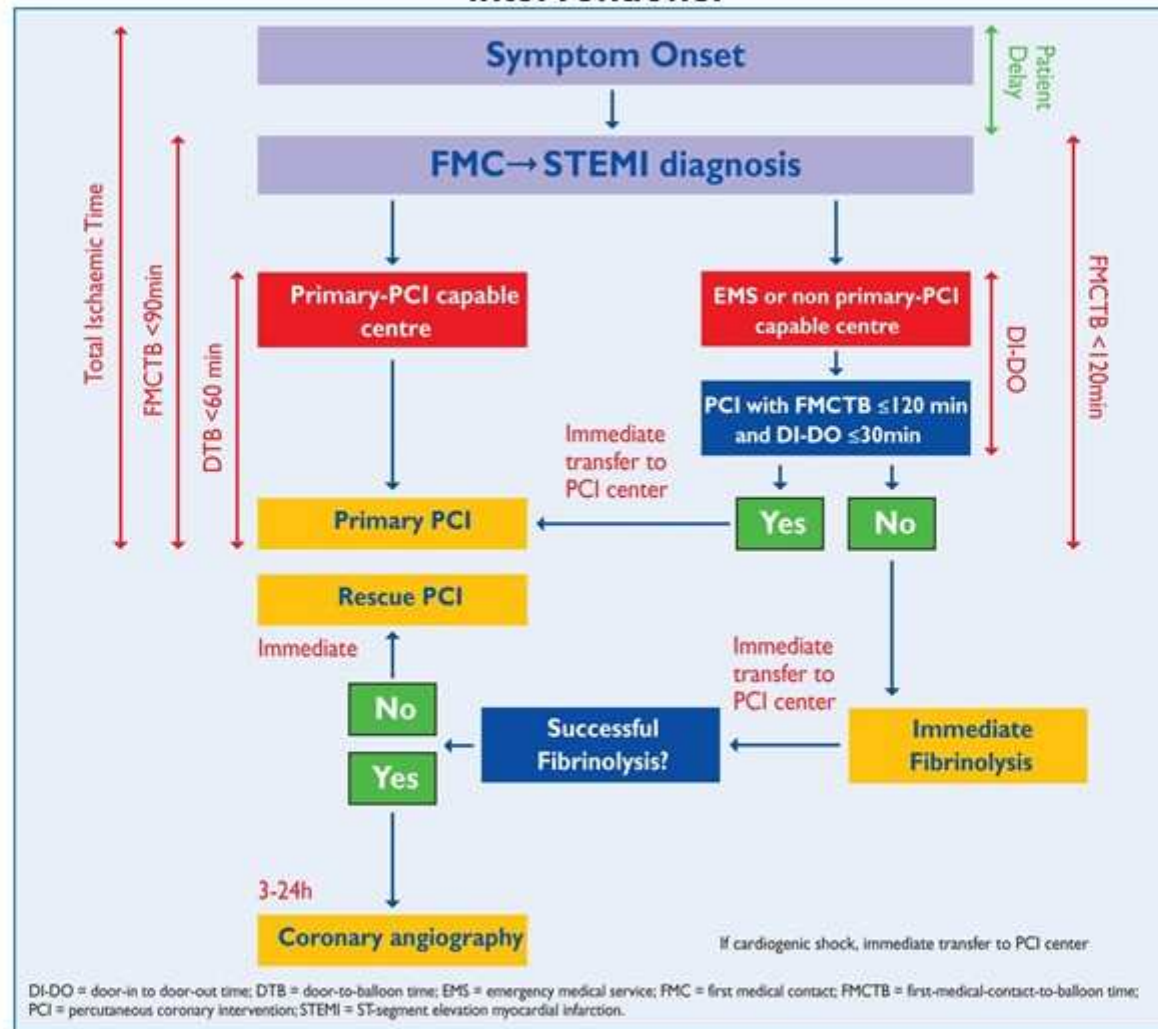
Huber K et al. The organization, function, and outcomes of ST-elevation myocardial infarction networks worldwide: current state, unmet needs and future directions. *Eur Heart J* 2014; 35: 1526-32.

Components of delay in STEMI and ideal time intervals for intervention



All delays are related to FMC (first medical contact)

Organization of STEMI patient disposal describing pre- and in-hospital management and reperfusion strategies within 12 hours of first medical contact with ideal time interval for interventions.



Authors/Task Force members et al. Eur Heart J 2014;eurheartj.ehu278

Important delays and treatment goals in the management of acute STEMI

Delays	Target
Preferred for FMC to ECG and diagnosis.	≤ 10 min
Preferred for FMC to fibrinolysis ('FMC to needle').	≤ 30 min
Preferred for FMC to primary PCI ('door to balloon') in primary PCI hospitals.	≤ 60 min
Preferred for FMC to primary PCI.	≤ 90 min (≤ 60 min if early presenter with large area at risk) if this target cannot be met, consider fibrinolysis.
Acceptable for primary PCI rather than fibrinolysis.	≤ 120 min (≤ 90 min if early presenter with large area at risk) if this target cannot be met, consider fibrinolysis.
Preferred for successful fibrinolysis to angiography.	3-24 h

FMC = first medical contacts; PCI = percutaneous coronary intervention.

Arresto cardiaco extra-ospedaliero e infarto miocardico acuto

Cardiac arrest

Recommendations	Class	Level
All medical and paramedical personnel caring for a patient with suspected myocardial infarction must have access to defibrillation equipment and be trained in cardiac life support.	I	C
It is recommended to initiate ECG monitoring at the point of FMC in all patients with suspected myocardial infarction.	I	C
Therapeutic hypothermia is indicated early after resuscitation of cardiac arrest patients who are comatose or in deep sedation.	I	B
Immediate angiography with a view to primary PCI is recommended in patients with resuscitated cardiac arrest whose ECG shows STEMI.	I	B
Immediate angiography with a view to primary PCI should be considered in survivors of cardiac arrest without diagnostic ECG ST-segment elevation but with a high suspicion of ongoing infarction.	IIa	B

ECG = electrocardiogram; FMC = first medical contacts; PCI = percutaneous coronary intervention; STEMI = ST-segment elevation myocardial infarction.

Arresto cardiaco extra-ospedaliero

2014 ESC/EACTS Guidelines on myocardial revascularization

Recommendations	Class ^a	Level ^b	Ref ^c
In survivors of out-of-hospital cardiac arrest, immediate coronary angiography and revascularization, if appropriate, should be considered <u>irrespective of the ECG pattern</u> if no obvious non-coronary cause of the arrhythmia is present.	IIa	B	534–539, 567

Il trattamento dell'infarto

**2) Accenni di terapia farmacologica,
controllo glicemico, trattamento della
coronaropatia multivasale**

Inibitori P2Y12

ESC 2012

Recommendations	Class	Level
Antiplatelet therapy		
Aspirin oral or i.v. (if unable to swallow) is recommended	I	B
An ADP-receptor blocker is recommended in addition to aspirin. Options are:	I	A
• Prasugrel in clopidogrel-naïve patients, if no history of prior stroke/TIA, age < 75 years.	I	B
• Ticagrelor.	I	B
• Clopidogrel, preferably when prasugrel or ticagrelor are either not available or contraindicated.	I	C

Antiplatelet therapy with low dose aspirin (75-100 mg) is indicated indefinitely after STEMI.	I	A
In patients who are intolerant to aspirin, clopidogrel is indicated as an alternative to aspirin.	I	B
DAPT with a combination of aspirin and prasugrel or aspirin and ticagrelor is recommended (over aspirin and clopidogrel) in patients treated with PCI	I	A
DAPT with aspirin and an oral ADP receptor antagonist must be continued for up to 12 months after STEMI, with a strict minimum of:	I	C
• 1 month for patients receiving BMS;	I	C
• 6 months for patients receiving DES.	IIb	B

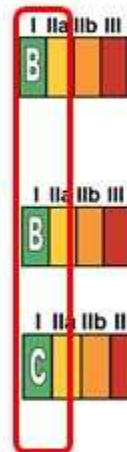
AHA/ACC 2013

	COR	LOE
Antiplatelet therapy		
Aspirin		
• 162- to 325-mg load before procedure	I	II
• 81- to 325-mg daily maintenance dose (indefinite)*	I	A
• 81 mg daily is the preferred maintenance dose*	IIa	B
P2Y₁₂ inhibitors		
Loading doses		
• Clopidogrel: 600 mg as early as possible or at time of PCI	I	B
• Prasugrel: 60 mg as early as possible or at time of PCI	I	B
• Ticagrelor: 180 mg as early as possible or at time of PCI	I	B
Maintenance doses and duration of therapy		
DES placed: Continue therapy for 1 y with:		
• Clopidogrel: 75 mg daily	I	II
• Prasugrel: 10 mg daily	I	B
• Ticagrelor: 90 mg twice a day*	I	B
BMS† placed: Continue therapy for 1 y with:		
• Clopidogrel: 75 mg daily	I	B
• Prasugrel: 10 mg daily	I	B
• Ticagrelor: 90 mg twice a day*	I	B
DES placed		
• Clopidogrel, prasugrel, or ticagrelor* continued beyond 1 y	IIb	C
• Patients with STEMI with prior stroke or TIA: prasugrel	III	B

Beta Bloccanti

ESC 2012

Recommendations	Class	Level
Oral treatment with beta-blockers should be considered during hospital stay and continued thereafter in all STEMI patients without contraindications.	IIa	B
Oral treatment with beta-blockers is indicated in patients with heart failure or LV dysfunction.	I	A
Intravenous beta-blockers must be avoided in patients with hypotension or heart failure.	III	B
Intravenous beta-blockers should be considered at the time of presentation in patients without contraindications, with high blood pressure, tachycardia and no signs of heart failure.	IIa	B



AHA/ACC 2013

Oral beta blockers should be initiated in the first 24 hours in patients with STEMI who do not have any of the following: signs of HF, evidence of a low output state, increased risk for cardiogenic shock,* or other contraindications to use of oral beta blockers (PR interval >0.24 seconds, second- or third-degree heart block, active asthma, or reactive airways disease).

Beta blockers should be continued during and after hospitalization for all patients with STEMI and with no contraindications to their use.

Patients with initial contraindications to the use of beta blockers in the first 24 hours after STEMI should be reevaluated to determine their subsequent eligibility.

It is reasonable to administer intravenous beta blockers at the time of presentation to patients with STEMI and no contraindications to their use who are hypertensive or have ongoing ischemia.

Inibitori del Sistema Renina Angiotensina Aldosterone

ESC 2012

ACE inhibitors are indicated starting within the first 24 h of STEMI in patients with evidence of heart failure, LV systolic dysfunction, diabetes or an anterior infarct.	I	A
An ARB, preferably valsartan, is an alternative to ACE inhibitors in patients with heart failure or LV systolic dysfunction, particularly those who are intolerant to ACE inhibitors.	I	B
ACE inhibitors should be considered in all patients in the absence of contraindications.	IIa	A
Aldosterone antagonists, e.g. eplerenone, are indicated in patients with an ejection fraction $\leq 40\%$ and heart failure or diabetes, provided no renal failure or hyperkalaemia.	I	B

AHA/ACC 2013



An ACE inhibitor should be administered within the first 24 hours to all patients with STEMI with anterior location, HF, or EF less than or equal to 0.40, unless contraindicated.



An ARB should be given to patients with STEMI who have indications for but are intolerant of ACE inhibitors.



An aldosterone antagonist should be given to patients with STEMI and no contraindications who are already receiving an ACE inhibitor and beta blocker and who have an EF less than or equal to 0.40 and either symptomatic HF or diabetes mellitus.



ACE inhibitors are reasonable for all patients with STEMI and no contraindications to their use.

Statine

ESC 2012

A fasting lipid profile must be obtained in all STEMI patients, as soon as possible after presentation.	I	C
It is recommended to initiate or continue high dose statins early after admission in all STEMI patients without contraindication or history of intolerance, regardless of initial cholesterol values.	I	A
Reassessment of LDL-cholesterol should be considered after 4-6 weeks to ensure that a target value of ≤ 1.8 mmol/L (70 mg/dL) has been reached.	IIa	C



AHA/ACC 2013

High-intensity statin therapy should be initiated or continued in all patients with STEMI and no contraindications to its use.

It is reasonable to obtain a fasting lipid profile in patients with STEMI, preferably within 24 hours of presentation.

Controllo glicemico

ESC 2012

Recommendations	Class	Level
Measurement of glycaemia is indicated at initial evaluation in all patients, and should be repeated in patients with known diabetes or hyperglycaemia.	I	C
Plans for optimal outpatient glucose control and secondary prevention must be determined in patients with diabetes before discharge.	I	C
The goals of glucose control in the acute phase should be to maintain glucose concentrations ≤ 11.0 mmol/L (200 mg/dL) while avoiding fall of glycaemia < 5 mmol/L (< 90 mg/dL). In some patients, this may require a dose-adjusted insulin infusion with monitoring of glucose, as long as hypoglycaemia is avoided.	IIa	B
A measurement of fasting glucose and HbA1c and, in some cases, a post-discharge oral glucose tolerance test should be considered in patients with hyperglycaemia but without a history of diabetes.	IIa	B
Routine glucose-insulin-potassium infusion is not indicated.	III	A

AHA/ACC 2013

- Blood glucose levels should be maintained below 180 mg/dL if possible while avoiding hypoglycemia.
- There is no established role for glucose-insulin-potassium infusions in patients with STEMI.

Coronaropatia multivasale

ESC/EACTS 2014

(GL on myocardial revascularization)

Staged revascularization of non-culprit lesions should be considered in STEMI patients with multivessel disease in case of symptoms or ischaemia within days to weeks after primary PCI.	IIa	B	235
Immediate revascularization of significant non-culprit lesions during the same procedure as primary PCI of the culprit vessel may be considered in selected patients.	IIb	B	267

AHA/ACC 2015

(Focused update on primary PCI)

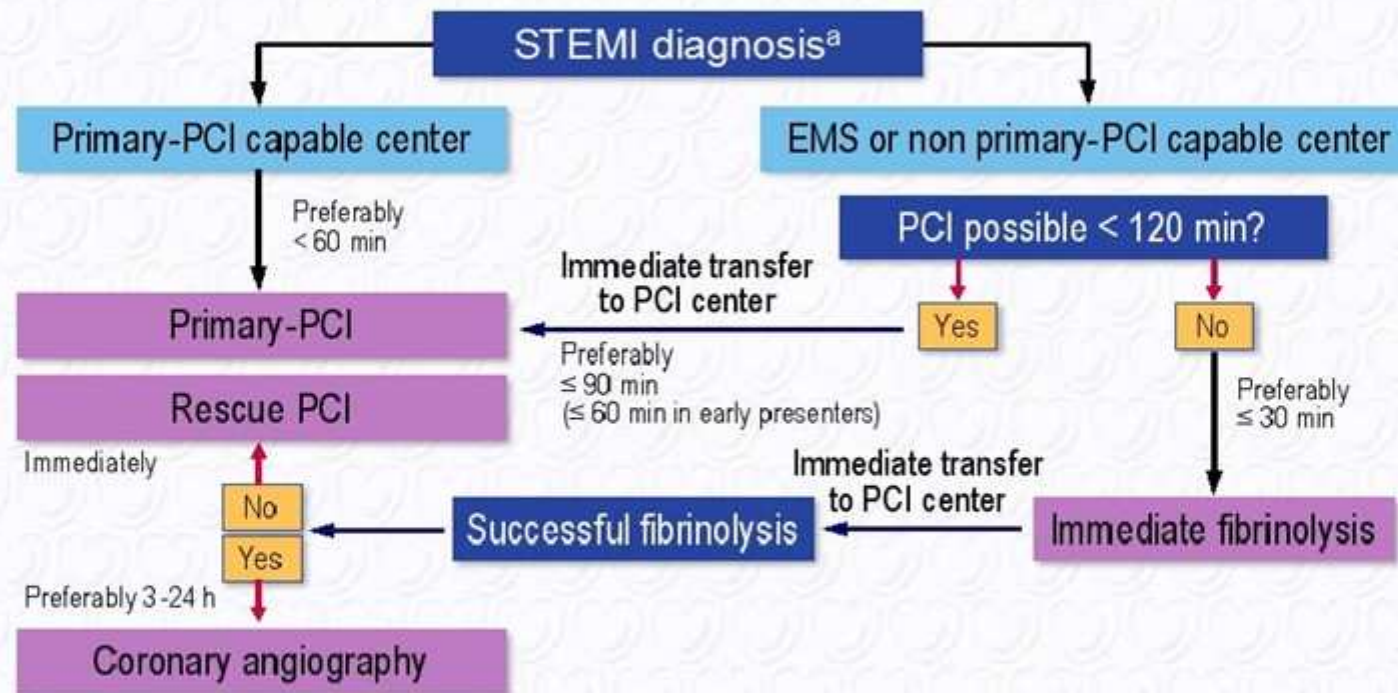
COR	LOE	Recommendation
IIb	B-R	PCI of a noninfarct artery may be considered in selected patients with STEMI and multivessel disease who are hemodynamically stable, either at the time of primary PCI or as a planned staged procedure. ¹

1. Modified recommendation from 2013 Guideline (changed class from III: Harm to IIb and expanded time frame in which multivessel PCI could be performed).

Grazie per l'attenzione



Prehospital and in-hospital management, and reperfusion strategies within 24 h of FMC



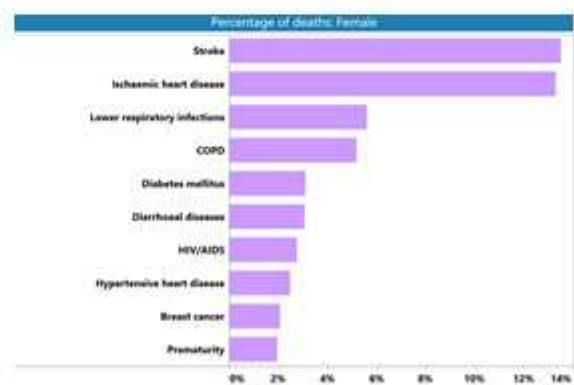
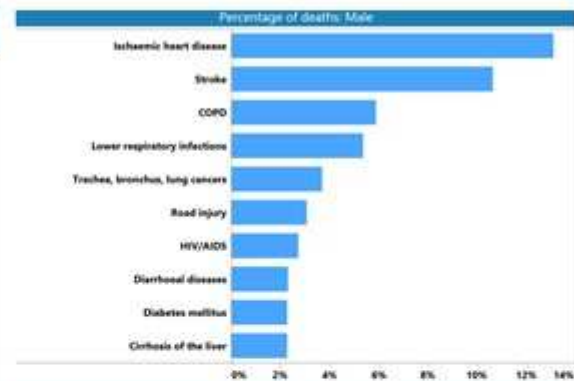
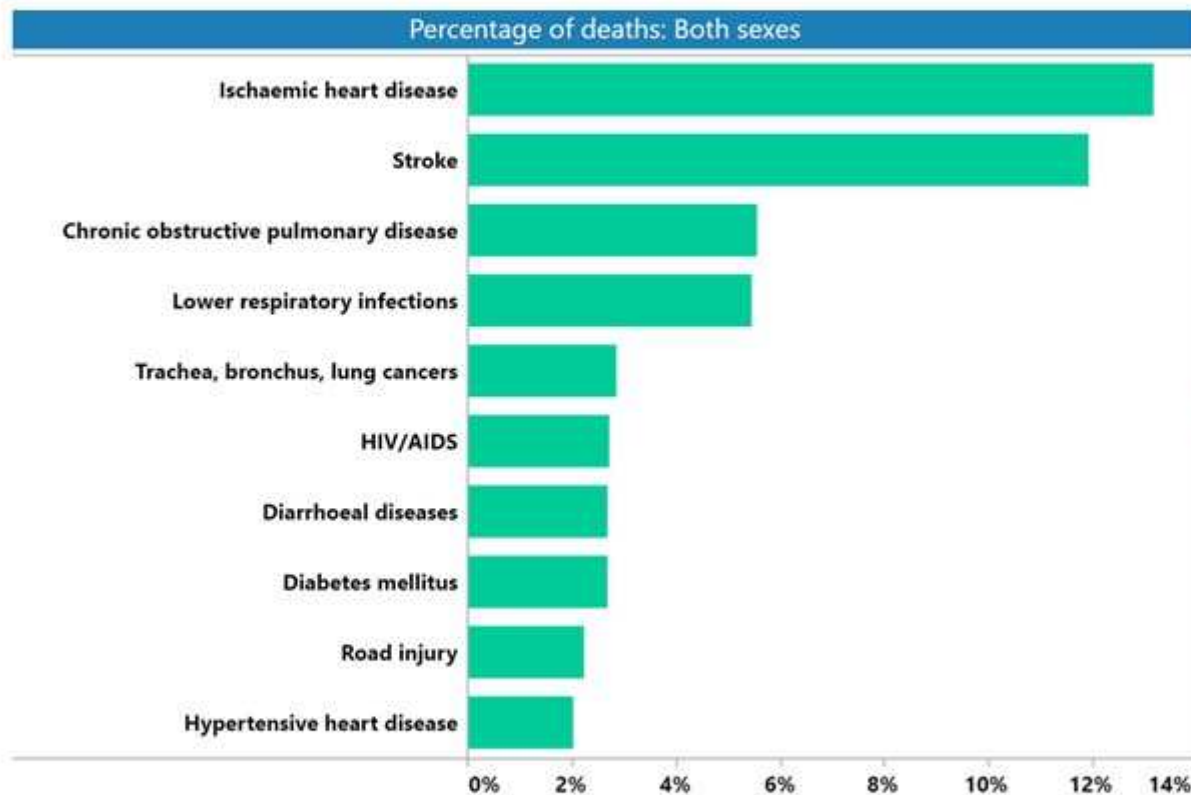
^a The time point the diagnosis is confirmed with patient history and ECG ideally within 10 min from the first medical contact (FMC). All delays are related to FMC (first medical contact).

Cath = catheterization laboratory; EMS = emergency medical system; FMC = first medical contact; PCI = percutaneous coronary intervention; STEMI = ST-segment elevation myocardial infarction.

Global Health Observatory (GHO) Data

Causes of death

Ten leading causes of death, 2012



World Heart Failure Alliance

Global Heart Failure
Awareness
Programme



GLOBAL HEART FAILURE
AWARENESS PROGRAMME



HEART FAILURE
ASSOCIATION
OF THE ESC



EUROPEAN
SOCIETY OF
CARDIOLOGY®

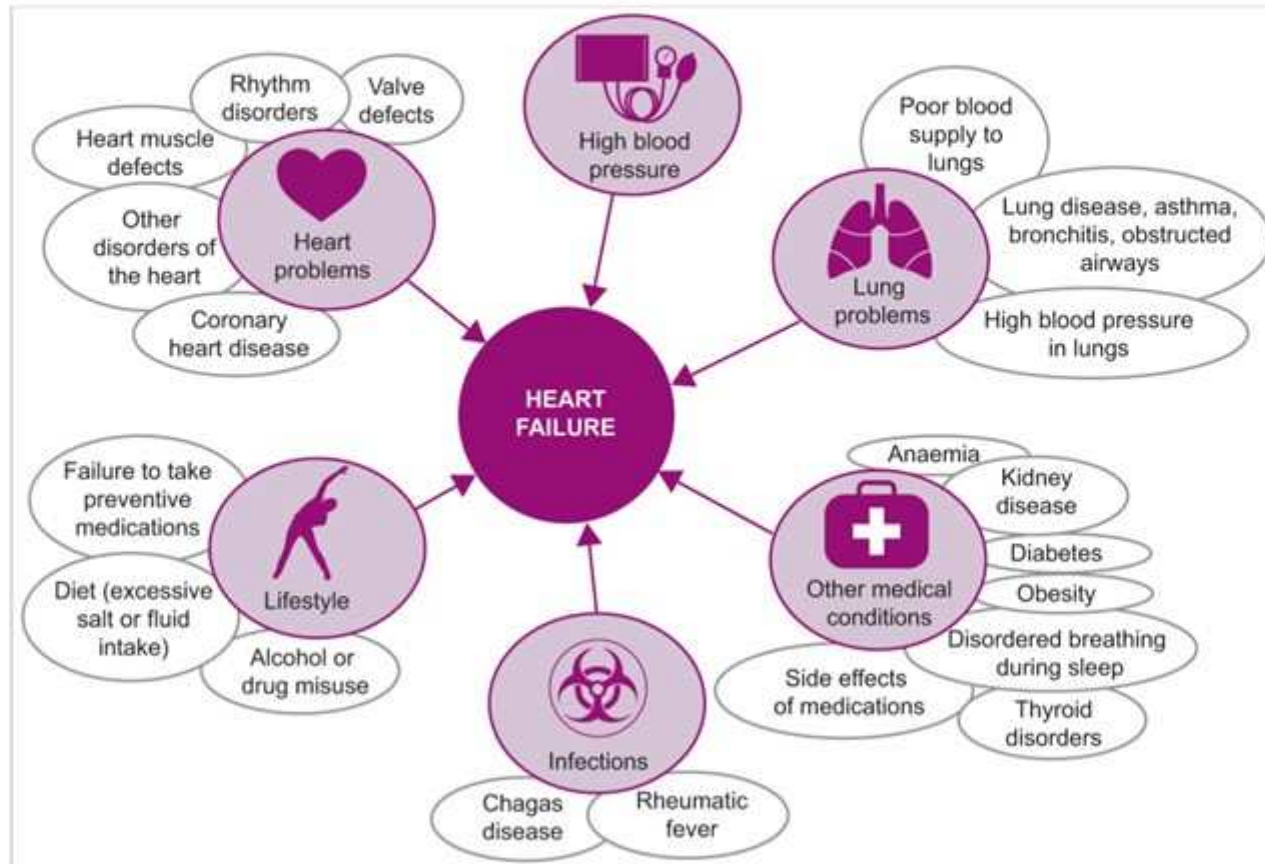


Figure 5. Common causes of heart failure.

Adapted from Cowie *et al.*, Improving care for patients with acute heart failure: before, during and after hospitalization, 2014,¹¹ with permission from Oxford PharmaGenesis™ Ltd.

Main challenges: heart failure hospitalization

>1 million

Annual hospitalizations in both the United States and Europe¹

1-4%

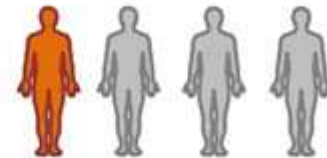
Heart failure hospitalizations as a percentage of total hospital admissions²

Up to 9/10 patients

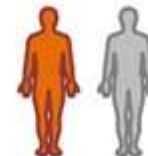
Hospitalized due to worsening chronic heart failure as compared with de novo heart failure³

5-10 days

Average length of hospital stay³



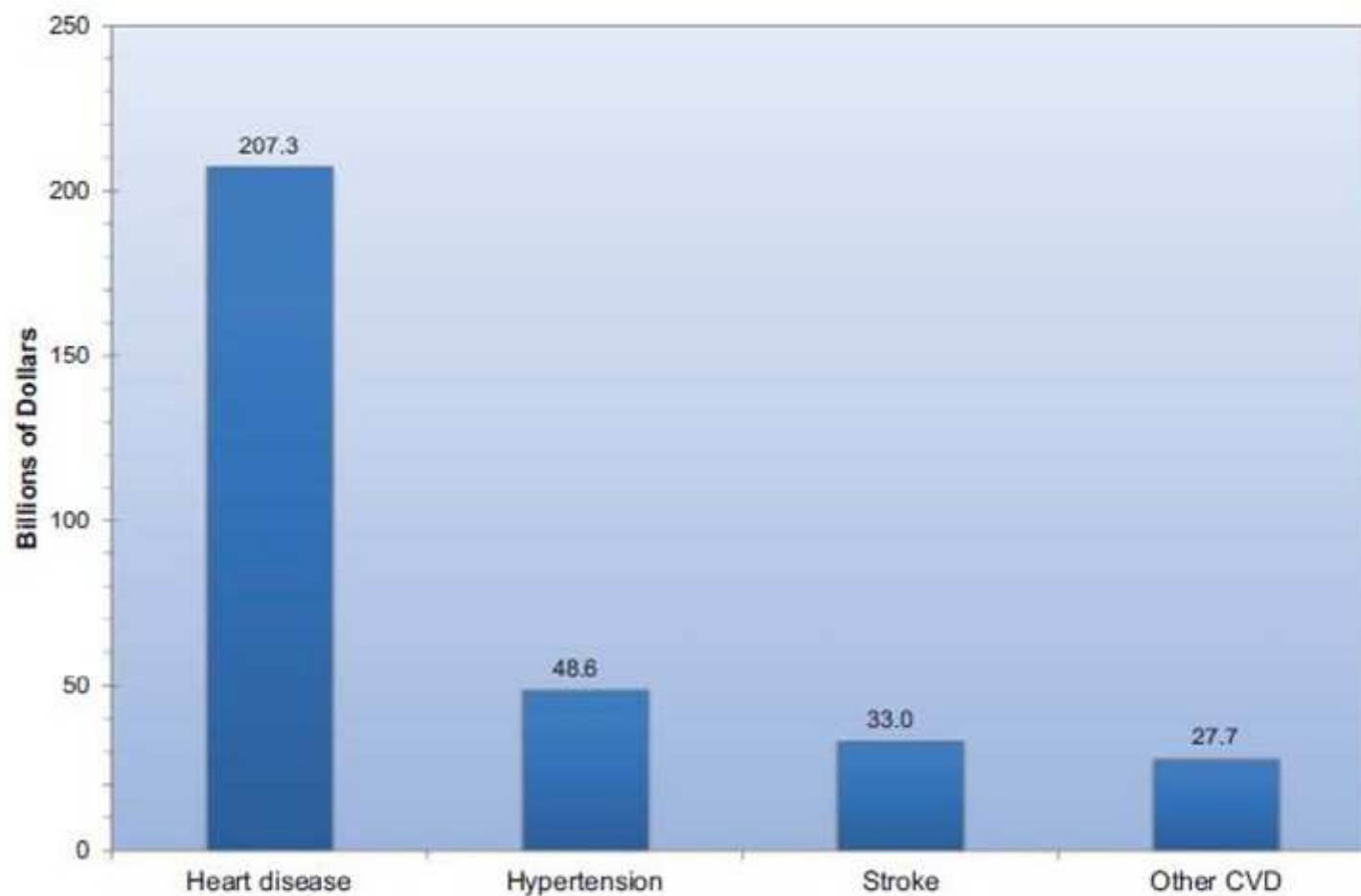
Almost 1 out of 4 hospitalized patients (24%) are rehospitalized for heart failure within the 30-day post discharge period⁴



Nearly 1 out of 2 patients (46%) are rehospitalized for heart failure within the 60-day post discharge period⁴

1. Ambrosy PA et al. The Global Health and Economic Burden of Hospitalizations for Heart Failure. Lessons Learned From Hospitalized Heart Failure Registries. *J Am Coll Cardiol.* 2014;63:1123-1133 2. Cowie MR et al. Improving care for patients with acute heart failure. 2014. Oxford PharmaGenesis. ISBN 978-1-903539-12-5. Available online at: <http://www.oxfordhealthpolicyforum.org/reports/acute-heart-failure/improving-care-for-patients-with-acute-heart-failure> . 3. Butler J, Braunwald E, Gheorghiade M. Recognizing worsening chronic heart failure as an entity and an end point in clinical trials. *JAMA.* 2014;312(8):789-90. 4. O'Connor CM et al. Causes of death and rehospitalization in patients hospitalized with worsening heart failure and reduce left ventricular ejection fraction: results from efficacy of vasopressin antagonism in heart failure outcome study with tolvaptan (EVEREST) program. *Am*

**Direct and indirect costs (in billions of dollars)
of major cardiovascular diseases and stroke (United States: 2011 to 2012)**



Source: National Heart, Lung, and Blood Institute.

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Mozaffarian D et al. Published online in *Circulation* Dec. 16, 2015

Logistics for networks

Table 8. Logistics of prehospital care

Recommendations	Class ^a	Level ^b	Ref. ^c
Ambulance teams must be trained and equipped to identify STEMI (with use of ECG recorders and telemetry as necessary) and administer initial therapy, including thrombolysis where applicable.	I	B	(43)
The prehospital management of STEMI patients must be based on regional networks designed to deliver reperfusion therapy expeditiously and effectively, with efforts made to make primary PCI available to as many patients as possible.	I	B	(47)
Primary PCI-capable centres must deliver a 24/7 service, be able to start primary PCI as soon as possible and within 60 min from the initial call.	I	B	(6, 52, 55)