METABOLISMO E RISCHIO CARDIOVASCOLARE NEL PAZIENTE CON ARTRITE PSORIASICA

Guglielmo Beccuti

S.C. Endocrinologia, Diabetologia e Metabolismo U.

A.O.U. Città della Salute e della Scienza di Torino

guglielmo.beccuti@unito.it

OUTLINE

- RISCHIO CARDIOVASCOLARE NELLA PsA
- RISCHIO CV: MECCANISMI
- EFFETTI CARDIOVASCOLARI DELLE TERAPIE PER PsA
- RACCOMANDAZIONI EULAR
- RISCHIO CV: STIMA, GESTIONE CLINICA, OBIETTIVI
- CONSAPEVOLEZZA E TERAPIA NELLA PRATICA CLINICA
- TERAPIA IPOLIPEMIZZANTE: NOVITÀ
- TERAPIA IPOGLICEMIZZANTE: NOVITÀ

Cardiovascular morbidity and mortality in ankylosing spondylitis and psoriatic arthritis

Jean W. Liew [a], Sofia Ramiro [b], Lianne S. Gensler [c, *]

Table 1
Cardiovascular mortality in PsA and AS.

x 1.5

Citation	Study type	Source	Comparator	Outcome collection/ definition	Effect size/result
PsA					
Wong 1997 [4]	Observational prospective cohort	University of Toronto PsA cohort	General population of Ontario	ICD-9 codes for cardiovascular death	SMR 1.33 (CI 7.72 –21.53)
Alhehoff 2010 [7]	Registry	Psoriasis cohort from Danish National Patient Register; n = 607 with PsA	General population of Denmark	ICD-10 codes for cardiovascular death	RR 1.84 (CI 1.11 –3.06)
Ogdie 2014 [9]	EHR database	UK THIN primary care database	General population of the UK	ICD-9 and -10 codes for cardiovascular death	aHR 1.09 (CI 0.91 –1.32)
Juneblad 2016 [10]	Registry	PsA cohort from a county (Skane) in Sweden	General population of Sweden	ICD-9 codes for cardiovascular death	SMR 1.64 (CI 1.02 –2.52)

Abbreviations: EHR = electronic health records; MI = myocardial infarction; ACS = acute coronary syndrome; IHD = ischemic heart disease; CVA = stroke; SPR = standardized prevalence ratios; SIR = standardized incidence ratio; IRR = incidence rate ratio; aHR = adjusted hazard ratio from multivariable analysis; aRR = adjusted relative risk from multivariable analysis.

Best Practice & Research Clinical Rheumatology 32 (2018) 369e389

Table 2
Cardiovascular disease and major adverse cardiac events in PsA.

x 1.5-2

Citation	Study type	Source	Comparator	Outcome definition	Effect size/result
IHD					
Gladman 2009 [17]	Observational prospective cohort	University of Toronto PsA cohort	General population of Canada	Clinical diagnosis of angina based on symptoms	SPR 1.97 (CI 1.24 –3.12)
MI					
Gladman 2009 [17]	Observational prospective cohort	University of Toronto PsA cohort	General population of Canada	Clinical diagnosis of MI: combination of symptoms, cardiac enzyme elevations, and EKG changes	SPR 2.57 (CI 1.73 –3.80)
Juneblad 2016 [10]	Observational prospective cohort	Swedish PsA cohort	General population of Sweden	ICD-9 codes for MI	SIR 0.60 (CI 0.34 –0.99)
Ogdie 2014 [126]	EHR database	UK THIN database	General population of the UK	READ codes for MI	aHR on DMARDs: 1.36 (CI 1.04–1.72) not on DMARDS: 1.36 (CI 1.01–1.84)
Bengtsson 2017 [19]	Registry	Swedish nationwide registries	General population of Sweden	ICD-10 codes for ACS	aHR 1.76 (CI 1.59 –1.95)

Abbreviations: EHR = electronic health records; MI = myocardial infarction; ACS = acute coronary syndrome; IHD = ischemic heart disease; CVA = stroke; SPR = standardized prevalence ratios; SIR = standardized incidence ratio; IRR = incidence rate ratio; aHR = adjusted hazard ratio from multivariable analysis; aRR = adjusted relative risk from multivariable analysis.

CVA	STROKE				
Gladman 2009 [17]	Observational prospective cohort	University of Toronto PsA cohort	General population of Canada	Clinical diagnosis based on neurological examination	SPR 0.91 (CI 0.34–2.43)
Juneblad 2016 [10]	Observational prospective cohort	Swedish PsA cohort	General population of Sweden	ICD-9 codes for CVA	SIR 0.59 (CI 0.32–0.99)
Ogdie 2014 [9]	EHR database	UK THIN database (primary care)	General population of the UK	READ codes for CVA	aHR on DMARDS: 1.33 (CI 1.03–1.71) not on DMARDS: 1.13 (CI 0.83–1.55)
Bengtsson 2017 [19]	Registry	Swedish nationwide registries	General population of Sweden	ICD-10 codes for composite stroke (CVA and TIA): I60-61, I63-64, and G45	aHR 1.34 (CI 1.22–1.48)
Combined MACE					
Lauper 2018 [20]	Registry	Swiss Clinical Quality Management Registry	Swiss RA population	MI, CVA, or CV death	Adjusted IRR 0.93 (CI 0.51–1.69) Adjusted prevalence ratio 0.98 (CI 0.58–1.61)
Cooksey 2018 [21]	EHR database	Welsh Secure Anonymised Information Linkage (SAIL) databank	General population of Wales	MI, CVA, or CV death	HR 1.5 (CI 0.9–2.5)

Abbreviations: EHR = electronic health records; MI = myocardial infarction; ACS = acute coronary syndrome; IHD = ischemic heart disease; CVA = stroke; SPR = standardized prevalence ratios; SIR = standardized incidence ratio; IRR = incidence rate ratio; aHR = adjusted hazard ratio from multivariable analysis; aRR = adjusted relative risk from multivariable analysis.

Table 4
Cardiovascular risk factors in PsA.

x 1.5

Citation	Study type	Source	Comparator	Effect size/Result
Diabetes				
Husted 2011 [35]	Prospective cohort	University of Toronto PsA cohort	Psoriasis	OR 2.03 (CI 0.85–4.81)
Eder 2017 [37]	Prospective cohort	University of Toronto PsA cohort	General population	SPR 1.43 (CI 1.2–1.7)
Gulati 2016 [38]	Population-based study	Norway – Nord Trondelag Health Study 3 (HUNT)	General population	p = 0.16
Jafri 2017 [40]	Registry	UK THIN primary care database	General population	aOR 1.38 (CI 1.31–4.50)
Dubreuil 2014 [48]	Registry	UK THIN primary care database	General population	aHR 1.33 (CI 1.09–1.61)
Labitigan 2014 [39]	Registry, cross-sectional analysis	CORRONA registry	RA	aOR 1.44 (CI 1.07–2.28)
Dreiher 2013 [46]	Claims database	Israel–Clalit database	General population	females: OR 1.60 (CI 1.02–2.52) males: OR 0.71 (CI 0.42–1.22)
Solomon 2009 [49]	Claims database	British Columbia insurance claims database	General population	aHR 1.4 (CI 1.3–1.5)
Radner 2017 [47]	Claims database	US Medicare insurance claims database	General population	IRR 1.14 (CI 1.03–1.26)

Hypertension	x 1.5-2			
Husted 2011 [35]	Prospective cohort	University of Toronto PsA cohort	Psoriasis	aOR 2.17 (CI 1.22–3.83)
Gulati 2016 [38]	Population-based study	Norway–Nord Trondelag Health Study 3 (HUNT)	General population	aOR 2.17 (CI 1.23–3.83)
Jafri 2017 [40]	Registry	UK THIN primary care database	General population	Prevalence: aOR 1.31 (CI 1.26–1.37) Incidence: aHR 1.31 (CI 1.23–1.39)
Labitigan 2014 [39]	Registry, cross-sectional analysis	CORRONA registry	RA	aOR 1.09 (CI 0.81–1.47)
Radner 2017 [47]	Claims database	US Medicare insurance claims database	General population	IRR 1.17 (CI 1.11–1.24)

Dyslipidemia	x 1.3			
Husted 2011 [35]	Prospective cohort	University of Toronto PsA cohort	Psoriasis	aOR 0.76 (CI 0.38–1.51)
Jafri 2017 [40]	Registry	UK THIN primary care database	General population	Prevalence: aOR 1.23 (CI 1.18–1.29) Incidence: aHR 1.24 (CI 1.16–1.34)
Labitigan 2014 [39]	Registry, cross-sectional analysis	CORRONA registry	RA	aOR 1.51 (CI 1.15–1.98)
Radner2017 [47]	Claims database	US Medicare insurance claims database	General population	IRR 1.10 (CI 1.04–1.17)

Best Practice & Research Clinical Rheumatology 32 (2018) 369e389

Obesity	x 1.5			
Husted 2011 [35]	Prospective cohort	University of Toronto PsA cohort	Psoriasis	aOR 1.29 (CI 0.82–2.04)
Eder 2017 [36]	Case–control study	University of Toronto PsA cohort	Psoriasis	aOR 1.77 (CI 1.23–2.56)
Gulati 2016 [38]	Population-based study	Norway–Nord Trondelag Health Study 3 (HUNT)	General population	$p < 0.0001$
Labitigan 2014 [39]	Registry, cross-sectional analysis	CORRONA registry	RA	aOR 1.19 (CI 0.90–1.57)
Radner 2017 [47]	Claims database	US Medicare insurance claims database	General population	IRR 1.25 (CI 1.14–1.36)
Metabolic syndrome	x 2			
Labitigan 2014 [39]	Registry, cross-sectional analysis	CORRONA registry	RA	aOR 1.44 (CI 1.05–1.96)
Mok 2011 [59]	Cross-sectional study	Hong Kong single-center outpatient cohort	General population	aOR 2.69 (CI 1.60–4.50)
Tobacco use				
Gulati 2016 [38]	Population-based study	Norway–Nord Trondelag Health Study 3 (HUNT)	General population	$p = 0.02$
Labitigan 2014 [39]	Registry, cross-sectional analysis	CORRONA registry	General population	$p = 0.02$

DATI EPIDEMIOLOGICI: SINTESI

CONDIZIONE CLINICA	ASSOCIAZIONE CON PsA
MORTALITA' CARDIOVASCOLARE	+
MALATTIA CV	+
STROKE	-
DIABETE	+
IPERTENSIONE	+
DISLIPIDEMIA	+
OBESITA'	+
SINDROME METABOLICA	+

x 1.5-2

- RISCHIO CARDIOVASCOLARE NELLA PsA
- **RISCHIO CV: MECCANISMI**
- EFFETTI CARDIOVASCOLARI DELLE TERAPIE PER PsA
- RACCOMANDAZIONI EULAR
- RISCHIO CV: STIMA, GESTIONE CLINICA, OBIETTIVI
- CONSAPEVOLEZZA E TERAPIA NELLA PRATICA CLINICA
- TERAPIA IPOLIPEMIZZANTE: NOVITÀ
- TERAPIA IPOGLICEMIZZANTE: NOVITÀ

FIGURE 2 | The concept of the "psoriatic march." This hypothesis suggests that psoriasis is a systemic inflammatory condition, as numerous biomarkers of inflammation are elevated in the patients' blood compartment. Functional consequences are insulin resistance, evidenced by an increased HOMA-IR (homeostasis assessment of insulin resistance), and endothelial dysfunction, resulting in increased vascular stiffness. This provides the basis for atherosclerosis, observable through analysis of vessel wall composition *via* CTs or ultrasound. Depending on the sites of atherosclerosis, major cardiovascular events such as myocardial infarction and stroke result from this. This "backbone" (red, bold) may be developed further by adding additional "modules": insulin resistance has been shown to alter epidermal homeostasis (red, fine). Obesity, causing a state of systemic inflammation as well, is a known risk factor for psoriasis and may induce the phenotype (orange, bold). Whether systemic anti-inflammatory therapy is capable of reducing the patients' cardiovascular risk through reducing insulin resistance and endothelial dysfunction is still a matter of debate (green).

Frontiers in Immunology, 2018

Int. J. Mol. Sci. 2018;19,1890

Hyperlipidaemia and cardiovascular disease

Table 1. Effects of inflammation on lipids, lipoproteins, apolipoproteins[a]

	HDL-related, antiatherogenic	ApoB-related, atherogenic
Lipids	↓HDL-C	↑Triglycerides ↓Total cholesterol ↓LDL-C
Lipoproteins, apolipoproteins	↓ApoA1 ↓Small HDL particles	↑Total VLDL particles, ↑Lp(a) ↑Small LDL particles (cholesterol-depleted)
		↑?ApoB, total LDL particles, IDL particles Small, medium, large VLDL particles

ApoA1, apolipoprotein A1; ApoB, Apolipoprotein B; HDL-C, HDL cholesterol; LDL-C, LDL cholesterol; Lp(a), Lipoprotein (a).
[a]Well established effects of inflammation are bolded.

Mackey, Curr Opin Lipidol 2019

ESTABLISHED IN 1812 SEPTEMBER 21, 2017 VOL. 377 NO. 12

The NEW ENGLAND JOURNAL of MEDICINE

Antiinflammatory Therapy with Canakinumab for Atherosclerotic Disease

P.M. Ridker, B.M. Everett, T. Thuren, J.G. MacFadyen, W.H. Chang, C. Ballantyne, F. Fonseca, J. Nicolau, W. Koenig, S.D. Anker, J.J.P. Kastelein, J.H. Cornel, P. Pais, D. Pella, J. Genest, R. Cifkova, A. Lorenzatti, T. Forster, Z. Kobalava, L. Vida-Simiti, M. Flather, H. Shimokawa, H. Ogawa, M. Dellborg, P.R.F. Rossi, R.P.T. Troquay, P. Libby, and R.J. Glynn, for the CANTOS Trial Group*

A Primary End Point with Canakinumab, 50 mg, vs. Placebo

No. at Risk						
Placebo	3344	3141	2973	2632	1266	210
Canakinumab	2170	2057	1950	1713	762	47

B Primary End Point with Canakinumab, 150 mg, vs. Placebo

No. at Risk						
Placebo	3344	3141	2973	2632	1266	210
Canakinumab	2284	2151	2057	1849	907	207

C Primary End Point with Canakinumab, 300 mg, vs. Placebo

No. at Risk						
Placebo	3344	3141	2973	2632	1266	210
Canakinumab	2263	2149	2038	1819	938	199

D Key Secondary End Point with Canakinumab, 150 mg, vs. Placebo

No. at Risk						
Placebo	3344	3107	2921	2578	1238	206
Canakinumab	2284	2135	2039	1824	892	201

Modulation of the interleukin-6 signalling pathway and incidence rates of atherosclerotic events and all-cause mortality: analyses from the Canakinumab Anti-Inflammatory Thrombosis Outcomes Study (CANTOS)

Paul M. Ridker[1,2]*, Peter Libby[2], Jean G. MacFadyen[1], Tom Thuren[3], Christie Ballantyne[4], Francisco Fonseca[5], Wolfgang Koenig[6], Hiroaki Shimokawa[7], Brendan M. Everett[1,2], and Robert J. Glynn[1], on behalf of the CANTOS Trial Group

ESC European Society of Cardiology

European Heart Journal (2018) **39**, 3499–3507
doi:10.1093/eurheartj/ehy310

No. at risk:						
Placebo	1597	1501	1411	1254	635	153
Canakinumab:						
IL-6 >=1.65 ng/L	1619	1524	1411	1211	562	123
IL-6 <1.65 ng/L	1617	1559	1501	1371	772	211

Figure 2 Cumulative incidence of myocardial infarction, stroke, and cardiovascular death (MACE) in CANTOS in the placebo group and in the combined canakinumab groups according to whether 3 months on-treatment IL-6 levels were above or below the on-treatment median value of 1.65 ng/L.

There was a slight increase in the risk of severe and fatal infections associated with canakinumab.

OUTLINE

- RISCHIO CARDIOVASCOLARE NELLA PsA
- RISCHIO CV: MECCANISMI
- **EFFETTI CARDIOVASCOLARI DELLE TERAPIE PER PsA**
- RACCOMANDAZIONI EULAR
- RISCHIO CV: STIMA, GESTIONE CLINICA, OBIETTIVI
- CONSAPEVOLEZZA E TERAPIA NELLA PRATICA CLINICA
- TERAPIA IPOLIPEMIZZANTE: NOVITÀ
- TERAPIA IPOGLICEMIZZANTE: NOVITÀ

The effects of tumour necrosis factor inhibitors, methotrexate, non-steroidal anti-inflammatory drugs and corticosteroids on cardiovascular events in rheumatoid arthritis, psoriasis and psoriatic arthritis: a systematic review and meta-analysis

Camille Roubille,[1] Vincent Richer,[2] Tara Starnino,[3] Collette McCourt,[4] Alexandra McFarlane,[5] Patrick Fleming,[6] Stephanie Siu,[7] John Kraft,[8] Charles Lynde,[8] Janet Pope,[7] Wayne Gulliver,[9] Stephanie Keeling,[5] Jan Dutz,[4] Louis Bessette,[10] Robert Bissonnette,[11] Boulos Haraoui[12]

Ann Rheum Dis 2015

Study	Compared trreatments (Tx1 vs. Tx2)	Endpoint	RR [95% CI]	Weight
Abuabara et al. 2011	Traditional systemics vs. no traditional systemics	MI	1.03 [0.79, 1.35]	13.9%
Abuabara et al. 2011	Biologics vs. no biologics	MI	1.04 [0.78, 1.38]	13.4%
Ahlehoff et al. 2012	Biologics vs. therapies other than biologics or MTX	Fatal CVD, MI or stroke	0.52 [0.18, 1.52]	2.7%
Ahlehoff et al. 2012	MTX vs. therapies other than biologics or MTX	Fatal CVD, MI or stroke	0.58 [0.29, 1.15]	5.4%
Chen et al. 2012	MTX vs. other nonbiologic antipsoriatic drugs	Hospitalization for new-onset IHD	0.97 [0.79, 1.19]	15.8%
Lan et al. 2012	MTX only vs. no MTX and no retinoid	CVE	0.50 [0.27, 0.93]	6.3%
Lan et al. 2012	Retinoid only vs. no MTX and no retinoid	CVE	0.70 [0.39, 1.23]	6.9%
Prodanowich et al. 2005	MTX vs. no MTX	Vascular diseases	0.78 [0.62, 0.98]	15.1%
Wu et al. 2012	TNFi vs. topical agents	MI	0.50 [0.32, 0.79]	9.2%
Wu et al. 2012	Oral agents/phototherapy vs. topical agents	MI	0.54 [0.38, 0.77]	11.5%
All			**0.75 [0.63, 0.91]**	**100.0%**

Heterogeneity: Tau² = 0.05; Chi² = 22.60, df = 9 (P = 0.007); I² = 60%
Test for overall effect: Z = 2.95 (P = 0.003)

Supplementary Figure 3. Meta-analyses of all cardiovascular events in psoriasis and/or psoriatic arthritis patients treated with systemic therapy in controlled studies. Size of data markers indicates relative weight of the study (from random-effects analysis). CI = confidence interval; CVE = cardiovascular events; IHD = ischemic heart disease; MI = myocardial infarction; RR = relative risk.

Systemic therapy was associated with a significant decrease in risk of all CVEs in Pso/PsA (RR, 0.75; 95% CI 0.63 to 0.91; p=0.003)

- RISCHIO CARDIOVASCOLARE NELLA PsA
- RISCHIO CV: MECCANISMI
- EFFETTI CARDIOVASCOLARI DELLE TERAPIE PER PsA
- **RACCOMANDAZIONI EULAR**
- RISCHIO CV: STIMA, GESTIONE CLINICA, OBIETTIVI
- CONSAPEVOLEZZA E TERAPIA NELLA PRATICA CLINICA
- TERAPIA IPOLIPEMIZZANTE: NOVITÀ
- TERAPIA IPOGLICEMIZZANTE: NOVITÀ

EULAR recommendations for cardiovascular disease risk management in patients with rheumatoid arthritis and other forms of inflammatory joint disorders: 2015/2016 update

eular
fighting rheumatic & musculoskeletal diseases together

Table 1 Overarching principles and recommendations

	Level of evidence	Strength of recommendation	Level of agreement (SD)
Overarching principles A. Clinicians should be aware of the higher risk for CVD in patients with RA compared with the general population. This may also apply to AS and PsA. B. The rheumatologist is responsible for CVD risk management in patients with RA and other IJD. C. The use of NSAIDs and corticosteroids should be in accordance with treatment-specific recommendations from EULAR and ASAS			
Recommendations			
1. Disease activity should be controlled optimally in order to lower CVD risk in all patients with RA, AS or PsA	2b-3	B	9.1 (1.3)
2. CVD risk assessment is recommended for all patients with RA, AS or PsA at least once every 5 years and should be reconsidered following major changes in antirheumatic therapy	3–4	C	8.8 (1.1)
3. CVD risk estimation for patients with RA, AS or PsA should be performed according to national guidelines and the SCORE CVD risk prediction model should be used if no national guideline is available	3–4	C–D	8.7 (2.1)
4. TC and HDLc should be used in CVD risk assessment in RA, AS and PsA and lipids should ideally be measured when disease activity is stable or in remission. Non-fasting lipids measurements are also perfectly acceptable	3	C	8.8 (1.2)
5. CVD risk prediction models should be adapted for patients with RA by a 1.5 multiplication factor, if this is not already included in the model	3–4	C	7.5 (2.2)
6. Screening for asymptomatic atherosclerotic plaques by use of carotid ultrasound may be considered as part of the CVD risk evaluation in patients with RA	3–4	C–D	5.7 (3.9)
7. Lifestyle recommendations should emphasise the benefits of a healthy diet, regular exercise and smoking cessation for all patients	3	C	9.8 (0.3)
8. CVD risk management should be carried out according to national guidelines in RA, AS or PsA, antihypertensives and statins may be used as in the general population	3–4	C–D	9.2 (1.3)
9. Prescription of NSAIDs in RA and PsA should be with caution, especially for patients with documented CVD or in the presence of CVD risk factors	2a-3	C	8.9 (2.1)
10. Corticosteroids: for prolonged treatment, the glucocorticoid dosage should be kept to a minimum and a glucocorticoid taper should be attempted in case of remission or low disease activity; the reasons to continue glucocorticoid therapy should be regularly checked	3–4	C	9.5 (0.7)

AS, ankylosing spondylitis; ASAS, Assessment of Spondyloarthritis International Society; CVD, cardiovascular disease; EULAR, European League against Rheumatism; HDLc, high-density lipoprotein cholesterol; IJD, inflammatory joint disorder; NSAID, non-steroidal anti-inflammatory drug; PsA, psoriatic arthritis; RA, rheumatoid arthritis; SCORE, Systematic Coronary Risk Evaluation; TC, total cholesterol.

Overarching prinicples

A. Clinicians should be aware of the higher risk for CVD in patients with RA compared with the general population. This may also apply to AS and PsA.

B. The rheumatologist is responsible for CVD risk management in patients with RA and other IJD.

Important to note the responsibility concerns that's gets done, but not that this should be done by rheumatologists themselves!

C. The use of NSAIDs and corticosteroids should be in accordance with treatment-specific recommendations from EULAR and ASAS.

1.CONSAPEVOLEZZA
2.GESTIONE MULTIDISCIPLINARE

Recommendation 1

Disease activity should be controlled optimally in order to lower CVD risk in all patients with RA, AS or PsA.

Contribution of inflammation towards increased CV risk is less known in AS and PsA in comparison to RA

LoE: 2B-3

Recommendation 2

CVD risk assessment is recommended for all patients with RA, AS or PsA at least once every 5 years and should be reconsidered following major changes in antirheumatic therapy.

Screening every 5 years is in line with ESC guidelines*

LoE: 3-4

* Piepoli MF, Hoes AW, Agewall S, et al. 2016 European Guidelines on cardiovascular disease prevention in clinical practice: The Sixth Joint Task Force of the European Society of Cardiology and Other Societies on Cardiovascular Disease Prevention in Clinical Practice (constituted by representatives of 10 societies and by invited experts): developed with the special contribution of the European Association for Cardiovascular Prevention & Rehabilitation (EACPR).Eur Heart J 2016;37:2315–81.

Recommendation 3

CVD risk estimation for patients with RA, AS or PsA should be performed according to national guidelines and the SCORE CVD risk prediction model should be used if no national guideline is available.

Presently no validated disease specific CVD risk prediction models that accurately predict risk in RA are available

LoE: 3-4

Recommendation 4

TC and HDLc should be used in CVD risk assessment in RA, AS and PsA and lipids should ideally be measured when disease activity is stable or in remission. Non-fasting lipids measurements are also perfectly acceptable.

Patients with RA with active disease generally have lower serum TC and LDLc levels compared with the general population, while their CVD risk is elevated.

Measurement of TC and HDLc are perfectly acceptable in non-fasting state according to the 2016 European guidelines on CVD prevention*

LoE: 3

* Piepoli MF, Hoes AW, Agewall S, et al. 2016 European Guidelines on cardiovascular disease prevention in clinical practice: The Sixth Joint Task Force of the European Society of Cardiology and Other Societies on Cardiovascular Disease Prevention in Clinical Practice (constituted by representatives of 10 societies and by invited experts): developed with the special contribution of the European Association for Cardiovascular Prevention & Rehabilitation (EACPR).Eur Heart J 2016;37:2315–81.

Recommendation 5

CVD risk prediction models should be adapted for patients with RA by a 1.5 multiplication factor, if this is not already included in the model.

Based on all recent epidemiology, this multiplication factor is still the most evidence-based way of estimating CVD risk in patients with RA.

LoE: 3-4

Recommendation 6

Screening for asymptomatic atherosclerotic plaques by use of carotid ultrasound may be considered as part of the CVD risk evaluation in patients with RA.

The presence of carotid plaques is associated with poor CVD-free survival and is strongly linked to future acute coronary syndrome (ACS) in patients with RA

The level of agreement of this recommendation by the task force members was low

LoE: 3-4

Recommendation 7

Lifestyle recommendations should emphasize the benefits of a healthy diet, regular exercise, and smoking cessation for all patients.

There is accumulating data that structured exercise therapy has beneficial CVD effects in patients with RA

In RA, the positive effect of a Mediterranean diet may be mediated by the effect of this diet on disease activity. However, there is no specific evidence available on the effect of dietary modifications on CVD risk in patients with IJD. Therefore, national guidelines regarding a healthy diet as part of a healthy lifestyle were recommended

LoE: 3

Recommendation 8

CVD risk management should be carried out according to national guidelines in RA, AS or PsA, antihypertensives, and statins may be used as in the general population.

For the management of hypertension and hyperlipidaemia, there is no evidence that treatment thresholds/targets should differ in patients with IJD compared with the general population.

LoE: 3 - 4

Recommendation 9

Prescription of NSAIDs in RA and PsA should be with caution, especially for patients with documented CVD or in the presence of CVD risk factors.

There is evidence that NSAIDs might increase CVD risk in RA to a lesser extent in comparison to the general population than was previously thought. Hence, there is no evidence to be stricter with NSAID treatment in patients with RA than what is recommended for the general population

LoE: 2a-3

Recommendation 10

Corticosteroids: for prolonged treatment, the glucocorticoid dosage should be kept to a minimum and a glucocorticoid taper should be attempted in case of remission or low disease activity; the reasons to continue glucocorticoid therapy should be regularly checked.

Corticosteroids rapidly and effectively reduce inflammation in RA, but they have also been associated with an increased CVD risk, although the literature shows conflicting results.

There is no conclusive evidence about the long-term effects of corticosteroids, particularly in low daily dosage, on safety outcomes including CVD events in RA.

LoE: 3-4

OUTLINE

- RISCHIO CARDIOVASCOLARE NELLA PsA
- RISCHIO CV: MECCANISMI
- EFFETTI CARDIOVASCOLARI DELLE TERAPIE PER PsA
- RACCOMANDAZIONI EULAR
- **RISCHIO CV: STIMA, GESTIONE CLINICA, OBIETTIVI**
- CONSAPEVOLEZZA E TERAPIA NELLA PRATICA CLINICA
- TERAPIA IPOLIPEMIZZANTE: NOVITÀ
- TERAPIA IPOGLICEMIZZANTE: NOVITÀ

2016 EUROPEAN CVD PREVENTION IN CLINICAL PRACTICE

European Heart Journal 2016;37:2315–2381- doi:10.1093/eurheartj/ehw106

EUROPEAN SOCIETY OF CARDIOLOGY®

How to estimate cardiovascular risk

Recommendations	Class	Level
Total CV risk estimation, using a risk estimation system such as SCORE, is recommended for adults >40 years of age, unless they are automatically categorised as being at *high-risk* or *very high-risk* based on documented CVD, DM (>40 years of age), kidney disease or highly elevated single risk factor.	I	C

European Heart Journal 2016;37:2315–2381-doi:10.1093/eurheartj/ehw106

EUROPEAN SOCIETY OF CARDIOLOGY®

Current cardiovascular disease risk (1)

	Framingham	SCORE	ASSIGN – SCORE	QRISK & QRISK	PROCAM	Pooled Cohort Studies Equations	CUORE	Globorisk
Data	Prospective studies: Framingham Heart Study and Framingham offspring study. Latest version includes both.	12 pooled prospective studies.	SHHEC Prospective Study.	QRESEARCH database.	Prospective study.	4 Pooled prospective studies ARIC, CHS CARDIA Framingham (original and offspring studies).	CUORE	Derivation cohort: 8 pooled prospective studies - Atherosclerosis Risk in Communities, Cardiovascular Health Study, Framingham Heart Study original cohort and offspring cohort, Honolulu Program, Multiple Risk Factor Intervention Trial, Puerto Rico Heart Health Program, and Women's Health Initiative Clinical Trial.
Population	General population, Framingham, Massachusetts, USA. Baselines: 1968-1971, 1971-1975, 1984-1987	12 prospective studies from 11 European countries. Baselines: 1972–1991	Random sample from general population in Scotland, baseline: 1984–1987	Data collected from 1993–2008 from GP databases - imputation of missing data.	Healthy employees. Baseline: 1978-1995	Baselines 1987-89 (ARIC), 1990 and 1992–3 (CHS), 1985-6 (CARDIA), 1968-1971, 1971-1975, 1984-198 (Framingham)	1980s and 1990s	8 prospective studies from North America. Baselines: 1948–1993
Sample size	3969 men and 4522 women.	117 098 men and 88 080 women.	6540 men and 6757 women.	1.28 million (QRISK1) 2.29 million (QRISK2)	18 460 men and 8515 women.	11 240 white women, 9098 white men, 2641 African-American women and 1647 African-American men	7520 men and 13 127 women	33 323 men and 16 806 women.
Calculates	**10-year risk of CAD events** originally. Latest version: 10-year risk of CVD events. NCEP ATP III version: 10-year risk of hard coronary events.	**10-year risk of CVD mortality.**	**10-year risk of CVD events.**	**10-year risk of CVD events.** Lifetime risk.	Two separate scores calculate 10-year risks of **major coronary events and cerebral ischaemic events.**	**10-year risk for a first atherosclerotic CVD event. Lifetime risk.**	**10-year probability of developing a first major CV event (myocardial infarction or stroke)**	**10 year risk of fatal cardiovascular Disease.**

Current cardiovascular disease risk (2)

	Framingham	SCORE	ASSIGN – SCORE	QRISK & QRISK	PROCAM	Pooled Cohort Studies Equations	CUORE	Globorisk
Age range (years)	30–75	40–65	30–74	35–74	20–75	20–79	35–69	40-84
Variables	Sex, age, total cholesterol, HDL-C, SBP, smoking status, DM, hypertensive treatment.	Sex, age, total Cholesterol or total cholesterol/ HDL-C ratio, SBP, smoking status. Versions for use in high and low-risk Countries.	Sex, age, total cholesterol, HDL-C, SBP, smoking - no. cigs, DM, area based index of deprivation, family history.	QRISK1 - sex, age total cholesterol to HDL-C ratio, SBP, smoking status, DM, area based index of deprivation, family history, BMI, BP treatment, ethnicity and chronic diseases.	Age, sex, LDL-C, HDL-C, DM, smoking, SBP.	Age, sex, race (white or other/African American), total cholesterol, HDL-C, SBP, antihypertensive treatment, DM, smoking.	Age, sex, SBP, total cholesterol, HDL-C, antihypertensive therapy and smoking habit.	Age, sex, smoking, total cholesterol, DM, systolic BP.
Comments/ develop.	Latest version includes version based on non-laboratory values only, substituting BMI from lipid measurements.	National, updated Recalibrations.		QRISK2 includes interaction terms to adjust for the interactions between age and some of the Variables.	Recent change in the methods (Weibull) allows extension of risk estimation to women and broader age range.	Race specific beta coefficients for risk factors have been incorporated. Calculator shown to overestimate risk in external validations - this may indicate the need for recalibration in certain populations.		Recalibrations have been undertaken for 11 countries.
Recom. by guidelines	NCEP guidelines, Canadian CV guidelines, other national guidelines recommend adapted versions including New Zealand.	European Guidelines on CVD Prevention.	SIGN	NICE guidelines on lipid modification, QRISK Lifetime recommended by JBS3 guidelines.	International Task Force for Prevention of Coronary Disease Guidelines.	2013 AHA ACC Guideline on the assessment of CVD Risk.	**NOTA AIFA 13**	

SCORE chart illustrating how the approximate risk age can be read off the chart

Systolic blood pressure	Women, Non-smoker					Women, Smoker					Age	Men, Non-smoker					Men, Smoker				
	4	5	6	7	8	4	5	6	7	8		4	5	6	7	8	4	5	6	7	8
180	7	8	9	10	12	13	15	17	19	22	65	14	16	19	22	26	26	30	35	41	47
160	5	5	6	7	8	9	10	12	13	16		9	11	12	15	16	18	21	25	29	34
140	3	3	4	5	6	6	7	8	9	11		6	8	9	11	13	13	15	17	20	24
120	2	2	3	3	4	4	5	5	6	7		4	5	6	7	9	9	10	12	14	17
180	4	4	5	6	7	8	9	10	11	13	60	9	11	13	15	18	18	21	24	28	33
160	3	3	3	4	5	5	6	7	8	9		6	7	9	10	12	12	14	17	20	24
140	2	2	2	3	3	3	4	5	5	6		4	5	6	7	9	8	10	12	14	17
120	1	1	2	2	2	2	3	3	4	4		3	3	4	5	6	6	7	8	10	12
180	2	2	3	3	4	4	5	5	6	7	55	6	7	8	10	12	12	13	16	19	22
160	1	2	2	2	3	3	3	4	4	5		4	5	6	7	8	8	9	11	13	16
140	1	1	1	1	2	2	2	2	3	3		3	3	4	5	6	5	6	8	9	11
120	1	1	1	1	1	1	1	2	2	2		2	2	3	3	4	4	4	5	6	8
180	1	1	1	2	2	2	2	3	3	4	50	4	4	5	6	7	7	8	10	12	14
160	1	1	1	1	1	1	2	2	2	3		2	3	3	4	5	5	6	7	8	10
140	0	1	1	1	1	1	1	1	1	2		2	2	2	3	3	3	4	5	6	7
120	0	0	1	1	1	1	1	1	1	1		1	1	2	2	2	2	3	3	4	5
180	0	0	0	0	0	0	0	0	1	1	40	1	1	1	2	2	2	2	3	3	4
160	0	0	0	0	0	0	0	0	0	0		1	1	1	1	1	1	2	2	2	3
140	0	0	0	0	0	0	0	0	0	0		0	1	1	1	1	1	1	1	2	2
120	0	0	0	0	0	0	0	0	0	0		0	0	1	1	1	1	1	1	1	1

Cholesterol (mmol/L)

150 200 250 300 mg/dl

SCORE

- 15% and over
- 10%-14%
- 5%-9%
- 3%-4%
- 2%
- 1%
- <1%

10-year risk of fatal CVD in populations at **High CVD risk**

The risk of this 40 year old male smoker with risk factors is the same (3%) as that of a 60 year old man with ideal risk factor levels–therefore his risk age is 60 years.

© ESC 2016

www.escardio.org/guidelines

EUROPEAN SOCIETY OF CARDIOLOGY®

European Heart Journal 2016;37:2315–2381-doi:10.1093/eurheartj/ehw106

Risk categories

Very high-risk	Subjects with any of the following: • Documented CVD, clinical or unequivocal on imaging. Documented clinical CVD includes previous AMI, ACS, coronary revascularization and other arterial revascularization procedures, stroke and TIA, aortic aneurysm and PAD. Unequivocally documented CVD on imaging includes significant plaque on coronary angiography or carotid ultrasound. It does NOT include some increase in continuous imaging parameters such as intima–media thickness of the carotid artery. • DM with target organ damage such as proteinuria or with a major risk factor such as smoking or marked hypercholesterolaemia or marked hypertension. • Severe CKD (GFR <30 mL/min/1.73 m^2). • A calculated SCORE ≥10%.
High-risk	Subjects with: • Markedly elevated single risk factors, in particular cholesterol >8 mmol/L (>310 mg/dL) (e.g. in familial hypercholesterolaemia) or BP ≥180/110 mmHg. • Most other people with DM (with the exception of young people with type 1 DM and without major risk factors that may be at low or moderate risk). • Moderate CKD (GFR 30–59 mL/min/1.73 m^2). • A calculated SCORE ≥5% and <10%.
Moderate-risk	SCORE is ≥1% and <5% at 10 years. Many middleaged subjects belong to this category.
Low-risk	SCORE <1%.

European Heart Journal 2016;37:2315–2381-doi:10.1093/eurheartj/ehw106

EUROPEAN SOCIETY OF CARDIOLOGY®

Risk factor goals and target levels

Smoking	No exposure to tobacco in any form.
Diet	Low in saturated fat with a focus on wholegrain products, vegetables, fruit and fish.
Physical activity	At least 150 minutes a week of moderate aerobic PA (30 minutes for 5 days/week) or 75 minutes a week of vigorous aerobic PA (15 minutes for 5 days/week) or a combination thereof.
Body weight	BMI 20–25 kg/m². Waist circumference <94 cm (men) and or <80 cm (women).
Blood pressure	<140/90 mmHg.[a]
Lipid	
LDL [b] is the primary target	**Very high-risk: <1.8 mmol/L (<70 mg/dL)**, or a reduction of at least 50% if the baseline
	t least 50% if the baseline is
Non-HDL-C [b]	<2.6, <3.3 and <3.8 mmol/L (<100, <130 and <145 mg/dL) are recommended for very high, high and low to moderate risk subjects, respectively
HDL-C	No target but >1.0 mmol/L (>40 mg/dL) in men and >1.2 mmol/L (>45 mg/dL) in women indicate lower risk.
Triglycerides	No target but <1.7 mmol/L (<150 mg/dL) indicates lower risk and higher levels indicate a need to look for other risk factors.
Diabetes	HbA1c: <7% (<53 mmol/L).

OBIETTIVI PERSONALIZZATI SULLA BASE DEL PROFILO DI RISCHIO (nuovi obiettivi nelle LG Displidemia 2019)

a. The target can be higher in frail elderly patients, or lower in most patients with DM and in some (very) high risk patients without DM who can tolerate multiple blood pressure lowering drugs
b. A view was expressed that primary care physicians might prefer a single general LDL-C goal of 2.6 mmol/L.
c. Non-HDL-C is a reasonable and practical alternative target because it does not require fasting.
d. This is the general recommendation for those at very high risk. It should be noted that the evidence for patients with chronic kidney disease is less strong

- RISCHIO CARDIOVASCOLARE NELLA PsA
- RISCHIO CV: MECCANISMI
- EFFETTI CARDIOVASCOLARI DELLE TERAPIE PER PsA
- RACCOMANDAZIONI EULAR
- RISCHIO CV: STIMA, GESTIONE CLINICA, OBIETTIVI
- **CONSAPEVOLEZZA E TERAPIA NELLA PRATICA CLINICA**
- TERAPIA IPOLIPEMIZZANTE: NOVITÀ
- TERAPIA IPOGLICEMIZZANTE: NOVITÀ

NATURE REVIEWS | RHEUMATOLOGY

volume 14 | June 2018

COMORBIDITIES

NEWS & VIEWS

Optimization of CVD prevention in psoriatic arthritis

Anne Grete Semb and Silvia Rollefstad

Patients with psoriatic arthritis and other inflammatory joint diseases have a high risk of cardiovascular disease (CVD), but use relatively little preventive medication such as antihypertensive and lipid lowering agents. An unmet need exists for the optimization of CVD prevention in this high-risk patient population.

Refers to Eder, L. et al. Gaps in diagnosis and treatment of cardiovascular risk factors in patients with psoriatic disease: an international multicenter study. *J. Rheumatol.* **45**, 378–384 (2018).

Gaps in Diagnosis and Treatment of Cardiovascular Risk Factors in Patients with Psoriatic Disease: An International Multicenter Study

Lihi Eder, Paula Harvey, Vinod Chandran, Cheryl F. Rosen, Jan Dutz, James T. Elder, Proton Rahman, Christopher T. Ritchlin, Sherry Rohekar, Richard Hayday, Snezana Barac, Joy Feld, Devy Zisman, and Dafna D. Gladman

The Journal of Rheumatology 2018; 45:3; doi:10.3899/jrheum.170379

59.2% of patients with hypertension were undertreated

Figure 2. Factors associated with undertreatment of hypertension. Values are OR (95% CI). PsC: psoriasis; PsA: psoriatic arthritis; NSAID: nonsteroidal antiinflammatory drugs.

65.6% of patients with dyslipidemia were undertreated

Figure 3. Factors associated with undertreatment of dyslipidemia. Values are OR (95% CI). PsC: psoriasis; PsA: psoriatic arthritis; NSAID: nonsteroidal antiinflammatory drugs.

The Journal of Rheumatology 2018; 45:3; doi:10.3899/jrheum.170379

Guideline recommended treatment to targets of cardiovascular risk is inadequate in patients with inflammatory joint diseases

Eirik Ikdahl [a,*,1], Grunde Wibetoe [a,1], Silvia Rollefstad [a], Anne Salberg [b], Kjetil Bergsmark [c], Tore K. Kvien [c], Inge C. Olsen [c], Dag Magnar Soldal [d], Gunnstein Bakland [e], Åse Lexberg [f], Bjørg Tilde Svanes Fevang [g], Hans Christian Gulseth [h], Glenn Haugeberg [d,i], Anne Grete Semb [a]

Fig. 1. a–b. Frequencies of indications for cardiovascular disease preventive drugs, proportions of patients treated with cardiovascular disease preventive drugs and rates of treatment goal attainment, across inflammatory joint disease entities. LLT: lipid lowering treatment, AntiHT: antihypertensive treatment, RA: rheumatoid arthritis, axSpA: ankylosing spondylitis, PsA: psoriatic arthritis, LDL-c: low-density lipoprotein cholesterol, BP: blood pressure. Crude data.

International Journal of Cardiology 274 (2019) 311–318

Performances of five risk algorithms in predicting cardiovascular events in patients with Psoriatic Arthritis: An Italian bicentric study

Luca Navarini[1], Domenico Paolo Emanuele Margiotta[1]*, Francesco Caso[2], Damiano Currado[1], Marco Tasso[2], Silvia Angeletti[3], Massimo Ciccozzi[3], Raffaele Scarpa[2], Antonella Afeltra[1], Luisa Costa[2]

Table 1. Items included in SCORE, CUORE, FRS, QRISK2, and RRS (grey bars).

	SCORE	CUORE	FRS	QRISK2	RRS
Age					
Sex					
Ethnicity					
Systolic blood pressure					
Total cholesterol					
HDL cholesterol					
Smoking status					
Diabetes					
Antihypertensive treatment					
Family history of CV disease					
Chronic kidney disease (stage 4 or 5)					
Atrial fibrillation					
Rheumatoid arthritis					
Body mass index					
High sensitivity C-reactive protein					

Navarini - Plos One 2018

SCORE
Observed or predected CV events (%)
40
35
30
25
20
15
10
5
0
1
2
3
4
5
6
Sextiles of predicted CV risk
Observed
Predicted

SCORE*1.5
Observed or predicted CV events (%)
40
35
30
25
20
15
10
5
0
1
2
3
4
5
6
Sextiles of predicted CV risk
Observed
Predicted

CUORE
Observed or predected CV events (%)
40
35
30
25
20
15
10
5
0
1
2
3
4
5
6
7
8
9
10
Deciles of predicted CV risk
Observed
Predicted

CUORE*1,5
Observed or predected CV events (%)
40
35
30
25
20
15
10
5
0
1
2
3
4
5
6
7
8
9
10
Deciles of predicted CV risk
Observed
Predicted

Up to 80% of CV events occurred in patients at "low risk" and up to 93% of CV events in patients at "low-intermediate risk".

Adaption of the CV risk algorithms according to EULAR indications did not provide improvement in discriminative ability and calibration in patients with PsA.

- RISCHIO CARDIOVASCOLARE NELLA PsA
- RISCHIO CV: MECCANISMI
- EFFETTI CARDIOVASCOLARI DELLE TERAPIE PER PsA
- RACCOMANDAZIONI EULAR
- RISCHIO CV: STIMA, GESTIONE CLINICA, OBIETTIVI
- CONSAPEVOLEZZA E TERAPIA NELLA PRATICA CLINICA
- **TERAPIA IPOLIPEMIZZANTE: NOVITÀ**
- TERAPIA IPOGLICEMIZZANTE: NOVITÀ

ESC European Society of Cardiology
European Heart Journal (2019) **00**, 1–78
doi:10.1093/eurheartj/ehz455

ESC/EAS GUIDELINES

2019 ESC/EAS Guidelines for the management of dyslipidaemias: *lipid modification to reduce cardiovascular risk*

The Task Force for the management of dyslipidaemias of the European Society of Cardiology (ESC) and European Atherosclerosis Society (EAS)

Intensity of lipid lowering treatment

Treatment	Average LDL-C reduction
Moderate intensity statin	≈ 30%
High intensity statin	≈ 50%
High intensity statin plus ezetimibe	≈ 65%
PCSK9 inhibitor	≈ 60%
PCSK9 inhibitor plus high intensity statin	≈ 75%
PCSK9 inhibitor plus high intensity statin plus ezetimibe	≈ 85%

How does PCSK9 work?

a) Secreted PCSK9 binds to LDLR on the liver cell surface and mediates the lysosomal degradation of the complex formed by PCSK9 - LDLR - LDL.

How does Inhibitors work?

enbühl S, et al. Unmet Needs in LDL-C Lowering: s Won't Do! Drugs. 2016 Aug;76(12):1175-90

Study	mAbs Events	mAbs N	placebo Events	placebo N	OR
MENDEL	2	45	0	45	5.49
LAPLACE-TIMI 57	4	158	1	157	4.13
YUKAWA	0	105	2	102	0.19
DESCARTES	2	473	0	239	2.55
LAPLACE-2	5	1117	2	558	1.25
RUTHERFORD-2	3	220	0	109	3.56
YUKAWA-2	0	202	1	202	0.33
ODYSSEY LONG TERM	27	1550	26	788	0.51
ODYSSEY COMBO I	6	207	3	107	1.04
ODYSSEY FHI	8	322	3	163	1.37
ODYSSEY FHII	2	167	1	81	0.97
OSLER-1 OSLER-2	29	2976	31	1489	0.46
ODYSSEY JAPAN	3	143	1	72	1.53
ODYSSEY HIGH FH	6	71	0	35	7.67
ODYSSEY CHOICE I	8	573	8	458	0.79
ODYSSEY CHOICE II	2	173	0	116	3.43
GLAGOV	59	484	74	484	0.73
FOURIER	1344	13784	1563	13780	0.83
ODYSSEY-KT	3	97	5	102	0.61
ODYSSEY OUTCOMES	1301	9462	1474	9462	0.84
Summary	**2814**	**32329**	**3195**	**28549**	**0.83 (0.78, 0.87)**
Test for heterogeneity	**p-value=0.44**				

Cardiovascular events with PCSK9 inhibitors: an updated meta-analysis of randomised controlled trials.
Pharmacol Res. 2019 May;143:143-150

OUTLINE

- RISCHIO CARDIOVASCOLARE NELLA PsA
- RISCHIO CV: MECCANISMI
- EFFETTI CARDIOVASCOLARI DELLE TERAPIE PER PsA
- RACCOMANDAZIONI EULAR
- RISCHIO CV: STIMA, GESTIONE CLINICA, OBIETTIVI
- CONSAPEVOLEZZA E TERAPIA NELLA PRATICA CLINICA
- TERAPIA IPOLIPEMIZZANTE: NOVITÀ
- **TERAPIA IPOGLICEMIZZANTE: NOVITÀ**

Management of hyperglycaemia in type 2 diabetes, 2018. A consensus report by the American Diabetes Association (ADA) and the European Association for the Study of Diabetes (EASD)

DECISION CYCLE FOR PATIENT-CENTRED GLYCAEMIC MANAGEMENT IN TYPE 2 DIABETES

GOALS OF CARE

- Prevent complications
- Optimise quality of life

ASSESS KEY PATIENT CHARACTERISTICS

- Current lifestyle
- Comorbidities i.e. ASCVD, CKD, HF
- Clinical characteristics i.e. age, HbA_{1c}, weight
- Issues such as motivation and depression
- Cultural and socio-economic context

CONSIDER SPECIFIC FACTORS WHICH IMPACT CHOICE OF TREATMENT

- Individualised HbA_{1c} target
- Impact on weight and hypoglycaemia
- Side effect profile of medication
- Complexity of regimen i.e. frequency, mode of administration
- Choose regimen to optimise adherence and persistence
- Access, cost and availability of medication

SHARED DECISION-MAKING TO CREATE A MANAGEMENT PLAN

- Involves an educated and informed patient (and their family/caregiver)
- Seeks patient preferences
- Effective consultation includes motivational interviewing, goal setting and shared decision-making
- Empowers the patient
- Ensures access to DSMES

AGREE ON MANAGEMENT PLAN

- Specify SMART goals:
  - **S**pecific
  - **M**easurable
  - **A**chievable
  - **R**ealistic
  - **T**ime limited

IMPLEMENT MANAGEMENT PLAN

- Patients not meeting goals generally should be seen at least every 3 months as long as progress is being made; more frequent contact initially is often desirable for DSMES

ONGOING MONITORING AND SUPPORT INCLUDING:

- Emotional well-being
- Check tolerability of medication
- Monitor glycaemic status
- Biofeedback including SMBG, weight, step count, HbA_{1c}, BP, lipids

REVIEW AND AGREE ON MANAGEMENT PLAN

- Review management plan
- Mutual agreement on changes
- Ensure agreed modification of therapy is implemented in a timely fashion to avoid clinical inertia
- Decision cycle undertaken regularly (at least once/twice a year)

ASCVD = Atherosclerotic Cardiovascular Disease
CKD = Chronic Kidney Disease
HF = Heart Failure
DSMES = Diabetes Self-Management Education and Support
SMBG = Self-Monitored Blood Glucose

Fig. 1 Decision cycle for patient-centred glycaemic management in type 2 diabetes

LA RIVOLUZIONE COPERNICANA NELLA DIABETOLOGIA

GLUCOSE-LOWERING MEDICATION IN TYPE 2 DIABETES: OVERALL APPROACH

FIRST-LINE THERAPY IS METFORMIN AND COMPREHENSIVE LIFESTYLE (INCLUDING WEIGHT MANAGEMENT AND PHYSICAL ACTIVITY)
IF HbA_{1c} ABOVE TARGET PROCEED AS BELOW

TO AVOID CLINICAL INERTIA REASSESS AND MODIFY TREATMENT REGULARLY (3–6 MONTHS)

ESTABLISHED ASCVD OR CKD

ASCVD PREDOMINATES

EITHER/OR

- GLP-1 RA with proven CVD benefit[1]
- SGLT2i with proven CVD benefit[1], if eGFR adequate[2]

If HbA_{1c} above target

If further intensification is required or patient is now unable to tolerate GLP-1 RA and/or SGLT2i, choose agents demonstrating CV safety:

- Consider adding the other class (GLP-1 RA or SGLT2i) with proven CVD benefit
- DPP-4i if not on GLP-1 RA
- Basal insulin[4]
- TZD[5]
- SU[6]

HF OR CKD PREDOMINATES

PREFERABLY
SGLT2i with evidence of reducing HF and/or CKD progression in CVOTs if eGFR adequate[3]

OR

If SGLT2i not tolerated or contraindicated or if eGFR less than adequate[2] add GLP-1 RA with proven CVD benefit[1]

If HbA_{1c} above target

- Avoid TZD in the setting of HF

Choose agents demonstrating CV safety:

- Consider adding the other class with proven CVD benefit[1]
- DPP-4i (not saxagliptin) in the setting of HF (if not on GLP-1 RA)
- Basal insulin[4]
- SU[6]

NO

WITHOUT ESTABLISHED ASCVD OR CKD

COMPELLING NEED TO MINIMISE HYPOGLYCAEMIA

DPP-4i	GLP-1 RA	SGLT2i[2]	TZD
If HbA_{1c} above target	**If HbA_{1c} above target**	**If HbA_{1c} above target**	**If HbA_{1c} above target**
SGLT2i[2] **OR** TZD	SGLT2i[2] **OR** TZD	GLP-1 RA **OR** DPP-4i **OR** TZD	SGLT2i[2] **OR** DPP-4i **OR** GLP-1 RA

If HbA_{1c} above target

Continue with addition of other agents as outlined above

If HbA_{1c} above target

Consider the addition of SU[6] **OR** basal insulin:

- Choose later generation SU with lower risk of hypoglycaemia
- Consider basal insulin with lower risk of hypoglycaemia[7]

COMPELLING NEED TO MINIMISE WEIGHT GAIN OR PROMOTE WEIGHT LOSS

EITHER/OR

- GLP-1 RA with good efficacy for weight loss[8]
- SGLT2i[2]

If HbA_{1c} above target

- SGLT2i[2]
- GLP-1 RA with good efficacy for weight loss[8]

If HbA_{1c} above target

If triple therapy required or SGLT2i and/or GLP-1 RA not tolerated or contraindicated use regimen with lowest risk of weight gain

PREFERABLY

DPP-4i (if not on GLP-1 RA) based on weight neutrality

If DPP-4i not tolerated or contraindicated or patient already on GLP-1 RA, cautious addition of:

- SU[6] • TZD[5] • Basal insulin

COST IS A MAJOR ISSUE[9-10]

- SU[6]
- TZD[10]

If HbA_{1c} above target

- TZD[10]
- SU[6]

If HbA_{1c} above target

- **Insulin therapy** basal insulin with lowest acquisition cost

OR

- Consider DPP-4i **OR** SGLT2i with lowest acquisition cost[10]

1. Proven CVD benefit means it has label indication of reducing CVD events. For GLP-1 RA strongest evidence for liraglutide > semaglutide > exenatide extended release. For SGLT2i evidence modestly stronger for empagliflozin > canagliflozin.
2. Be aware that SGLT2i vary by region and individual agent with regard to indicated level of eGFR for initiation and continued use
3. Both empagliflozin and canagliflozin have shown reduction in HF and reduction in CKD progression in CVOTs
4. Degludec or U100 glargine have demonstrated CVD safety
5. Low dose may be better tolerated though less well studied for CVD effects
6. Choose later generation SU with lower risk of hypoglycaemia
7. Degludec / glargine U300 < glargine U100 / detemir < NPH insulin
8. Semaglutide > liraglutide > dulaglutide > exenatide > lixisenatide
9. If no specific comorbidities (i.e. no established CVD, low risk of hypoglycaemia and lower priority to avoid weight gain or no weight-related comorbidities)
10. Consider country- and region-specific cost of drugs. In some countries TZDs relatively more expensive and DPP-4i relatively cheaper

CHOOSING GLUCOSE-LOWERING MEDICATION IN THOSE WITH ESTABLISHED ATHEROSCLEROTIC CARDIOVASCULAR DISEASE (ASCVD) OR CHRONIC KIDNEY DISEASE (CKD)

Use principles in Figure 1

TO AVOID CLINICAL INERTIA REASSESS AND MODIFY TREATMENT REGULARLY (3–6 MONTHS)

Use metformin unless contraindicated or not tolerated

If not at HbA_{1c} target:

- Continue metformin unless contraindicated (remember to adjust dose/stop metformin with declining eGFR)
- Add SGLT2i or GLP-1 RA with proven cardiovascular benefit[1] (See below)

If at HbA_{1c} target:

- If already on dual therapy, or multiple glucose-lowering therapies and not on an SGLT2i or GLP-1 RA, consider switching to one of these agents with proven cardiovascular benefit[1] (See below)

OR reconsider/lower individualised target and introduce SGLT2i or GLP-1 RA

OR reassess HbA_{1c} at 3 month intervals and add SGLT2i or GLP-1 RA if HbA_{1c} goes above target

ASCVD predominates

GLP-1 RA with proven CVD benefit[1]

EITHER/ OR

SGLT2i with proven CVD benefit[1], if eGFR adequate[2]

Consensus recommendation

Among patients with type 2 diabetes who have established ASCVD, SGLT2 inhibitors or GLP-1 receptor agonists with proven cardiovascular benefit are recommended as part of glycaemic management (Figs 2 and 3).

Circulation

Zelniker - Circulation 2019

ORIGINAL RESEARCH ARTICLE

Comparison of the Effects of Glucagon-Like Peptide Receptor Agonists and Sodium-Glucose Cotransporter 2 Inhibitors for Prevention of Major Adverse Cardiovascular and Renal Outcomes in Type 2 Diabetes Mellitus

Systematic Review and Meta-Analysis of Cardiovascular Outcomes Trials

Figure 1. Meta-analysis of glucagon-like peptide 1 receptor agonist (GLP1-RA) and sodium-glucose cotransporter-2 inhibitor (SGLT2i) trials on the composite of myocardial infarction, stroke, and cardiovascular death stratified by the presence of atherosclerotic cardiovascular disease.
Forest plot showing the treatment estimates of each drug class in each subgroup using fixed effects. The summary estimates for each subgroup were modeled using random effects accounting for heterogeneity of the different drug classes. The test for subgroup differences was based on a F-test in a random effect metaregression using mixed effects accounting heterogeneity for drug class and patient population. The *P* value for subgroup differences was 0.028. For established atherosclerotic cardiovascular disease (ASCVD): GLP1-RA, Q statistic=10.89, *P*=0.028, I^2=63.3%; SGLT2i, Q statistic=0.94, *P*=0.63, I^2= 0%; total: Q statistic=11.85, *P*=0.11; and for multiple risk factor (MRF): GLP1-RA, Q statistic=0.24, *P*=0.89, I^2=0%; SGLT2i, Q statistic=0.033, *P*=0.86, I^2=0%; and total, Q statistic=0.34, *P*=0.99. HR indicates hazard ratio.

GLP1-RA per il diabete indotto da steroidi?

Diabetes Care. 2011 Feb; 34(2): 412–417.
Published online 2011 Jan 20. doi: 10.2337/dc10-1677
PMCID: PMC3024359
PMID: 21216851

Glucagon-Like Peptide-1 Receptor Agonist Treatment Prevents Glucocorticoid-Induced Glucose Intolerance and Islet-Cell Dysfunction in Humans

Daniël H. van Raalte, MD,[1] Renate E. van Genugten, MD,[1] Margot M.L. Linssen, MSC,[2] D. Margriet Ouwens, PHD,[3] and Michaela Diamant, MD, PHD[1]

Int J Mol Sci. 2019 Jul; 20(13): 3152.
Published online 2019 Jun 28. doi: 10.3390/ijms20133152
PMCID: PMC6651241
PMID: 31261624

Management of Diabetes Mellitus in Normal Renal Function, Renal Dysfunction and Renal Transplant Recipients, Focusing on Glucagon-Like Peptide-1 Agonist: A Review Based upon Current Evidence

Shang-Feng Tsai[1,2,3] and Cheng-Hsu Chen[1,2,*]

A1C reductions with antihyperglycemic agents

Network meta-analysis comparing antihyperglycemic drugs as add-on to metformin

Mean difference from placebo

***All statistically significant vs. placebo.** TZDs=thiazolidinediones; AGIs=alpha-glucosidase inhibitors; GLP-1=glucagon-like Peptide 1; DPP-4=dipeptidyl peptidase-4.

1. Liu, Sung-Chen *et al. Diab Obes & Metab* 2012; 14:810-820.

INTENSIFYING TO INJECTABLE THERAPIES

Consensus recommendation

In patients who need the greater glucose-lowering effect of an injectable medication, GLP-1 receptor agonists are the preferred choice to insulin. For patients with extreme and symptomatic hyperglycaemia, insulin is recommended (Fig. 7).

CONCLUSIONI

- CONSAPEVOLEZZA del **rischio CV (↑ nelle IJD)**
- CONSAPEVOLEZZA di un **bisogno di salute** non soddisfatto (*undertreatment*)
- **Gestione MULTIDISCIPLINARE** (ruolo del *team*)
- Terapia della Pso/PsA: riduzione del rischio CV (dati limitati)
- **Sottostima del rischio CV** mediante calcolatori
- **Controllo dei fattori cardio-endocrino-metabolici**: obiettivi personalizzati e disponibilità di terapie innovative e sicure

«70 anni… e non sentirli!»

Grazie per l'attenzione