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EXPERT OPINION

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ESC CVD Prevention Guidelines 2021: improvements, controversies, and opportunities

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The third iteration of the European Society of Cardiology (ESC) cardiovascular disease (CVD) prevention guidelines was recently released at the 2021 ESC Congress.[1] Following on from the original guidelines of 2012 and the update of 2016, these guidelines have been developed by the task force for CVD prevention in clinical practice with representatives of the ESC and 12 medical societies.

These guidelines reiterate the complexity of current knowledge in CVD prevention, and the need to move forward to more digitalized platforms for calculation of risk. At a high level, the focus seems to shift now towards targeting individuals' residual cardiovascular risk in a personalized manner to facilitate shared decision-making by the patient and their healthcare professional. There is much emphasis on 'tailored intervention' and 'individual level' targeting of risk. The central illustration of the guidelines summaries the various prevention groupings that have been arranged including apparently healthy people, those with established atherosclerotic cardiovascular disease (ASCVD), and those with specific risk conditions, such as diabetes, chronic kidney disease, and genetic conditions. The major change comes in the way risk is calculated and interpreted. From the 10-years risk of fatal cardiovascular event in the original ESC Systematic Coronary Risk Estimation (SCORE), we now move towards the 10-years risk of fatal and non-fatal cardiovascular event with ESC SCORE2. The ESC SCORE2 is meaningful in apparently healthy people aged 40–69 years, while for people aged ≥70 years, we should be using the Systematic Coronary Risk Estimation 2-Older Persons (SCORE2-OP). The risk estimation is further complicated by a geographical clustering that results in four separate SCORE2/SCORE2-OP risk assessment charts that change the risk levels based upon national CVD mortality rates. The SCORE2 or SCORE2-OP risk estimates must then be mapped onto the correct flow chart for 'CVD risk and risk factor treatment', which recommends certain therapies based upon the patient's 10-years CVD risk.

The question is: will clinicians embrace this at times impenetrable, complex system for risk calculation in daily clinical practice? For example, will practicing clinicians implement definitions like that of very high-risk individuals described as those with SCORE2 ≥ 7.5% for age under 50, SCORE2 ≥ 10% for age 50–69 or SCORE2-OP ≥15% for age ≥70 years, taking into account the geographical area where the patient lives? Is it time to move away from paper-based algorithms and risk calculation charts and enter the digital era, where complexity is replaced by the simplicity of user-friendly computerized platforms linked directly with the electronic patient records?

An important step forward is the introduction of the concept of 'lifetime risk'. This is a major advancement, although its calculation is still problematic due to the inconsistency of the life-long outcomes registries behind these scores. Lifetime risk can potentially guide early deployment of treatments independently of the patient age, which is a major problem in interpreting the clinical importance of the 10-years risk models in young individuals with risk factors that will inevitably lead to cardiovascular events decades after they are diagnosed.[2]

An interesting aspect of these guidelines is the inclusion of coronary artery calcium scoring or the use of plaque detection by carotid ultrasound as ways to improve risk classification (Class IIb), but not genetic scores or plasma biomarkers (Class III). Correctly the guidelines focus on the presence of disease, and this could be expanded in the future to include visualizing disease in the arterial bed of most relevance to cardiac mortality and events: the coronary arteries. Indeed, in patients with chest pain, coronary computed tomography angiography (CCTA) and detection of atherosclerosis reduced events by assisting deployment of treatments to those who need it.[3] In that context, measuring the disease activity by quantifying coronary inflammation, may be an additional way to recalibrate risk, at least in those with chest pain.[4,5] With the use of artificial intelligence,[6] we can now talk about recalculating a patient's personalized risk by using the ESC SCORE2 components, together with information extracted from routine coronary computed tomography angiography (atherosclerotic plaque burden and inflammation using perivascular Fat Attenuation Indexing), at least in individuals where a CCTA is performed with another clinical indication (i.e. chest pain). The recent results from the SCAPIS cohort[7] have demonstrated the value of performing CCTA also in asymptomatic individuals at a community level, for detecting coronary atherosclerosis.[4,8] So, incorporating imaging methodologies into the calculation of risk is certainly an area where future guidelines can focus.[4,8]

Beyond re-defining cardiovascular risk, the new ESC Prevention Guidelines are shifting our practice towards more aggressive management of CVD risk factors. Indeed, we now see a shift of the target blood pressure, coming down to 120–130 mmHg systolic for people 18–69 years old or 130–140 mmHg in ≥70 years old, and diastolic blood pressure <80 mmHg for all, being more aligned with the American Heart Association/American College of Cardiology (AHA/ACC) guidelines.[9] We also see new anti-diabetic treatments like GLP-1RA or SGLT2 inhibitors recommended in type 2 diabetic patients with ASCVD to reduce cardiovascular and cardiorenal events (Class I). SGLT2 inhibitors also received

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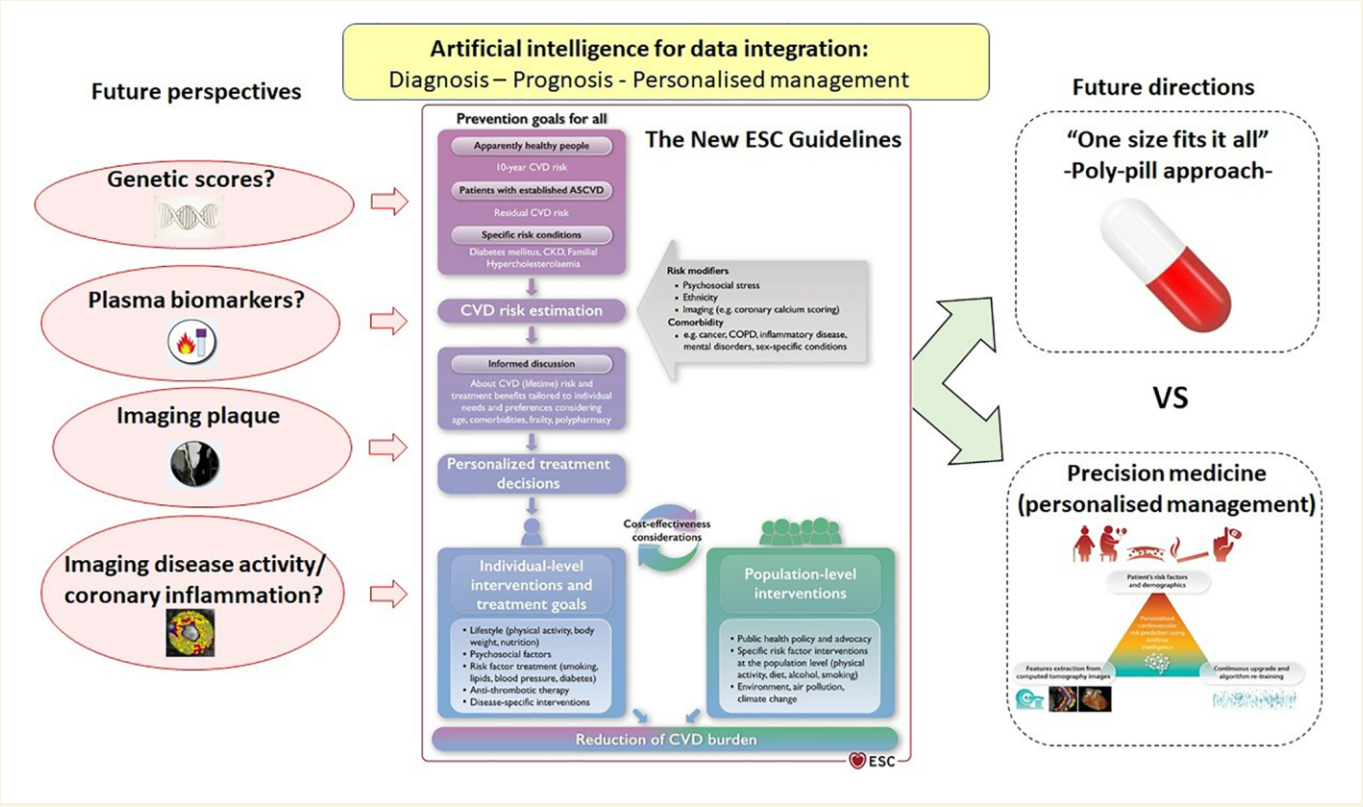

Figure 1 The new 2021 ESC Guidelines for CVD Prevention place personalization of risk assessment and therapy decisions as the ultimate goal within the introduction. A future update could include more prognostic information into the risk calculation, including genetic scores, plasma biomarkers of even imaging like coronary CT angiography. Of course, the fundamental question is whether this personalized risk prediction can be used to guide individual patient clinical management, or whether a blanket approach of prescribing a polypill without sophisticated risk assessment, would offer a good alternative, particularly in financially less developed countries. CVD, cardiovascular disease; ESC, European Society of Cardiology; HDL, high-density lipoprotein.

indication for type 2 diabetics with heart failure with reduced ejection fraction or chronic kidney disease (Class I). Another interesting aspect of the risk-modifying interventions is the indication for low-dose aspirin treatment in those people with diabetes or very high CVD risk (Class IIb). Finally, following the recent results of COLCOT[10] and LoDoCo2[11] trials, the new ESC guidelines recommend low dose of colchicine (0.5 mg daily) for secondary prevention particularly if other risk factors are insufficiently controlled or if recurrent CVD events occur under optimal therapy (Class IIb, level of evidence A). This is indeed an area where future guidelines could incorporate measures of assessing coronary inflammation using either plasma biomarkers[12–14] or advanced imaging methods[4,8] that could identify those who may respond better to anti-inflammatory treatments, avoiding unnecessary overmedication (*Figure 1*). On the other hand, however, there is an ongoing debate about the use of personalized medicine tools in different areas of the world, given that all these diagnostic tests with prognostic value are expensive; ideas like the use of the polypill[15] could offer a good alternative, as it can include untargeted treatment of all risk factors simultaneously. It may actually be time to consider inclusion of anti-inflammatory agents like colchicine, in the polypill of the future.

In summary, the new ESC guidelines on CVD prevention introduce new ways of calculating cardiovascular risk, and re-define what we call 'residual cardiovascular (or inflammatory) risk', providing new recommendations on how risk can be managed either by targeting the risk factors or directly the disease activity (i.e. inflammation or atherosclerotic plaque). However, the complexity of the new guidelines will make their implementation challenging, underlining the need for new digital tools (that could potentially utilize artificial intelligence modelling) to deliver this new knowledge into the hands of the practicing clinician.

Conflict of interest: C.A. is inventor of various patents in the space: patent PCT/GB2015/052359 and patent applications PCT/GB2017/053262, GB2018/1818049.7, GR20180100490, and GR20180100510, licensed through exclusive license to Caristo Diagnostics. C.A. is a founder, shareholder, and Director of Caristo Diagnostics, a CT image analysis company. H.W.W. has no relationships relevant to the contents of this article to disclose.

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References

1. Visseren FLJ, Mach F, Smulders YM, Carballo D, Koskinas KC, Bäck M, Benetos A, Biffi A, Boavida J-M, Capodanno D, Cosyns B, Crawford C, Davos CH, Desormais I, Di Angelantonio E, Franco OH, Halvorsen S, Hobbs FDR, Hollander M, Jankowska EA, Michal M, Sacco S, Sattar N, Tokgozoglu L, Tonstad S, Tsioufis KP, van Dis I, van Gelder IC, Wanner C, Williams B; ESC Scientific Document Group. 2021 ESC Guidelines on cardiovascular disease prevention in clinical practice: developed by the Task Force for cardiovascular disease prevention in clinical practice with representatives of the European Society of Cardiology and 12 medical societies with the special contribution of the European Association of Preventive Cardiology (EAPC). *Eur Heart J* 2021;**42**:3227–3337.

2. Patel RS, Lagord C, Waterall J, Moth M, Knapton M, Deanfield JE. Online self-assessment of cardiovascular risk using the Joint British Societies (JBS3)-derived heart age tool: a descriptive study. *BMJ Open* 2016;**6**:e011511.
3. Newby DE, Adamson PD, Berry C, Boon NA, Dweck MR, Flather M, Forbes J, Hunter A, Lewis S, MacLean S, Mills NL, Norrie J, Roditi G, Shah ASV, Timmis AD, van Beek EJR and Williams MC. Coronary CT Angiography and 5-Year Risk of Myocardial Infarction. N Engl J Med 2018;**379**:924–933.
4. Antonopoulos AS, Sanna F, Sabharwal N, Thomas S, Oikonomou EK, Herdman L, Margaritis M, Shirodaria C, Kampoli AM, Akoumianakis I, Petrou M, Sayeed R, Krasopoulos G, Psarros C, Ciccone P, Brophy CM, Digby J, Kelion A, Uberoi R, Anthony S, Alexopoulos N, Tousoulis D, Achenbach S, Neubauer S, Channon KM, Antoniades C. Detecting human coronary inflammation by imaging perivascular fat. *Sci Transl Med* 2017;**9**:eaal2658.
5. Oikonomou EK, Marwan M, Desai MY, Mancio J, Alashi A, Hutt Centeno E, Thomas S, Herdman L, Kotanidis CP, Thomas KE, Griffin BP, Flamm SD, Antonopoulos AS, Shirodaria C, Sabharwal N, Deanfield J, Neubauer S, Hopewell JC, Channon KM, Achenbach S, Antoniades C. Non-invasive detection of coronary inflammation using computed tomography and prediction of residual cardiovascular risk (the CRISP CT study): a post-hoc analysis of prospective outcome data. *Lancet* 2018;**392**:929–939.
6. Oikonomou EK, Siddique M, Antoniades C. Artificial intelligence in medical imaging: a radiomic guide to precision phenotyping of cardiovascular disease. *Cardiovasc Res* 2020;**116**:2040–2054.
7. Bergström G, Persson M, Adiels M, Björnson E, Bonander C, Ahlström H, Alfredsson J, Angerås O, Berglund G, Blomberg A, Brandberg J, Börjesson M, Cederlund K, Faire U, Duvernoy O, Ekblom Ö, Engström G, Engvall JE, Fagman E, Eriksson M, Erlinge D, Fagerberg B, Flinck A, Gonçalves I, Hagström E, Hjelmgren O, Lind L, Lindberg E, Lindqvist P, Ljungberg J, Magnusson M, Mannila M, Markstad H, Mohammad MA, Nystrom FH, Ostenfeld E, Persson A, Rosengren A, Sandström A, Själander A, Sköld MC, Sundström J, Swahn E, Söderberg S, Torén K, Östgren CJ, Jernberg T. Prevalence of subclinical coronary artery atherosclerosis in the general population. *Circulation* 2021;**144**:916–929.
8. Oikonomou EK, Antonopoulos AS, Schottlander D, Marwan M, Mathers C, Tomlins P, Siddique M, Klüner LV, Shirodaria C, Mavrogiannis MC, Thomas S, Fava A, Deanfield J, Channon KM, Neubauer S, Desai MY, Achenbach S, Antoniades C. Standardized measurement of coronary inflammation using cardiovascular computed tomography: integration in clinical care as a prognostic medical device. *Cardiovasc Res* 2021;**117**:2677–2690.
9. Whelton PK, Carey RM, Aronow WS, Casey DE, Collins KJ, Himmelfarb CD, DePalma SM, Gidding S, Jamerson KA, Jones DW, MacLaughlin EJ, Muntner P, Ovbiagele B, Smith SC, Spencer CC, Stafford RS, Taler SJ, Thomas RJ, Williams KA, Williamson JD, Wright JT. 2017 ACC/AHA/AAPA/ABC/ACPM/AGS/APhA/ASH/ASPC/NMA/PCNA Guideline for the prevention, detection, evaluation, and management of high blood pressure in adults. *Hypertension* 2018.**71**:e127–e248.
10. L'Allier PL, Tardif JC, Kouz S, Waters DD, Diaz R, Maggioni AP, Pinto FJ, Gamra H, Kiwan GS, Berry C, Lopez-Sendon JC, Koenig W, Blondeau L, Guertin MC, Roubille F; The COLCOT investigators. Low-dose colchicine in patients treated with percutaneous coronary interventions for myocardial infarction in the Colchicine Cardiovascular Outcomes Trial (COLCOT). *Eur Heart J* 2020;**41**:ehaa946.1556.
11. Nidorf SM, Fiolet ATL, Mosterd A, Eikelboom JW, Schut A, Opstal TSJ, The SHK, Xu X-F, Ireland MA, Lenderink T, Latchem D, Hoogslag P, Jerzewski A, Nierop P, Whelan A, Hendriks R, Swart H, Schaap J, Kuijper AFM, van Hessen MWJ, Saklani P, Tan I, Thompson AG, Morton A, Judkins C, Bax WA, Dirksen M, Alings M, Hankey GJ, Budgeon CA, Tijssen JGP, Cornel JH, Thompson PL. Colchicine in patients with chronic coronary disease. *N Engl J Med* 2020;**383**:1838–1847.
12. Antonopoulos AS, Angelopoulos A, Papanikolaou P, Simantiris S, Oikonomou EK, Vamvakaris K, Koumpoura A, Farmaki M, Trivella M, Vlachopoulos C, Tsioufis K, Antoniades C, Tousoulis D. Biomarkers of vascular inflammation for cardiovascular risk prognostication: a meta-analysis. *JACC Cardiovasc Imaging* 2021. https://doi.org/10.1016/j.jcmg.2021.09.014.
13. Libby P. Inflammation during the life cycle of the atherosclerotic plaque. *Cardiovasc Res* 2021;**117**:2525–2536.
14. Libby P, Mallat Z, Weyand C. Immune and inflammatory mechanisms mediate cardiovascular diseases from head to toe. *Cardiovasc Res* 2021;**117**:2503–2505.
15. Guzik TJ, Yusuf S. Leaders in cardiovascular research: Salim Yusuf. *Cardiovasc Res* 2020;**116**:e26–e28.

Authors

Biography: Charalambos Antoniades is a BHF Chair of Cardiovascular Medicine at University of Oxford and Consultant Cardiologist at Oxford University Hospitals. He was awarded his PhD title with hons on the genetics of premature myocardial infarction, and during his PhD studies, he won multiple Young Investigator award competitions, including those of the European Society of Cardiology (ESC) twice, the ISHR, and others. He has been awarded the Outstanding Achievement Award of the basic Cardiovascular Science Council of the European Society of Cardiology in 2016, a UK National clinical excellence award in 2020 and has given various named lectures. He is the Director of Acute Vascular Imaging Centre of the University of Oxford and the Deputy Head of the Division of Cardiovascular Medicine. He is also the Chair of the British Atherosclerosis Society. He is a Deputy Editor of Cardiovascular Research, and one of the founders of the Scientists of Tomorrow of the ESC. He is also founder and Chief Scientific Officer of Caristo Diagnostics, a University of Oxford spinout company.

His research is focused on the study of the cross-talk between adipose tissue and the cardiovascular system, with specific interest in the non-invasive imaging of inflammation. He directs the Oxford Heart Vessels and Fat programme, and coordinates large national flagship programmes (such as the UK C19-CRC) and international multicentre studies (e.g. ORFAN study). His research has led to the development of novel imaging biomarkers using Computed Tomography, with major role in cardiovascular risk prognosis.

Biography: Dr Henry W. West is a Clinical Fellow in Cardiology at the University of Oxford, UK, where he is also soon to complete his PhD with Professors Charalambos Antoniades and Keith Channonas a Rhodes Scholar. His work is concerned with the assessment of patient's individual risk for heart disease, including coronary artery disease, atrial fibrillation, and stroke. His expertise spans cardiovascular epidemiology, artificial intelligence in medical imaging, and biomarker discovery.