

**The 2018 ESC/ESH Hypertension Guideline and the 2019 NICE Hypertension Guideline, how and why they differ.**

**Terry McCormack, Rebecca Boffa, Nicholas Jones, Serena Carville, Richard J McManus**

Following the impressive results of the SPRINT study published in 2015 (1), international hypertension guideline committees have gradually updated their advice. In 2017 the American College of Cardiology and American Heart Association (ACC/AHA) were the first to do so (2), followed by the European Society of Cardiology and European Society of Hypertension (ESC/ESH) in 2018 (3), and most recently the National Institute for Health and Care Excellence (NICE), who published their ‘Hypertension in Adults’ guideline in August 2019 (4). These three influential guidelines will inform global practice, yet whilst agreeing on many points there are also important differences in their recommendations. Here we focus on the European perspective, introducing the headline changes and then asking how and why the NICE guidelines differ from those of the ESC/ESH.

The ESC/ESH guidelines reiterate the importance of reducing blood pressure (BP) below 140/90mmHg for all patients but go further to suggest, where tolerated, that systolic blood pressure (SBP) for those aged under 65 should be reduced to between 120 and 129mmHg. The recommended treatment threshold was retained at an SBP of 140mmHg, and recommended treatment for people with diabetes if BP is  $\geq 140/90$ mmHg but with a target of  $<130/80$ mmHg. In terms of treatment, ESC/ESH recommend a 3-step approach with single pill dual therapy if SBP is  $\geq 150$ mmHg and a single pill triple therapy if this is insufficient to obtain control. ESC/ESH also advocate low dose spironolactone for resistant hypertension, where triple therapy is unsuccessful.

The updated NICE guideline continues to recommend treating to a threshold and target BP of 140/90mmHg, as opposed to the lower treatment targets recommended by the ESC/ESH. Much of the guideline remains little changed from the 2011 guideline CG127 (5), with the major change being to reduce the risk threshold for treatment in uncomplicated stage 1 hypertension to 10% ten-year cardiovascular risk (previously 20%). The recommended treatment pathway remains similar to the previous guideline, with monotherapy at step 1 retained. Step 2 and 3 recommendations were amended so that medication choice focused on patient preferences. Similar to ESC/ESH, NICE recommends spironolactone, other diuretics and alpha- or beta-blockers for resistant hypertension. Guidance for hypertension in those with diabetes was included in the NICE hypertension guideline for the first time, having previously fallen into the remit of the diabetes guideline. A patient decision aid accompanies the NICE treatment recommendations.

To understand how such differences can occur between the NICE and ESC/ESH guidelines, it is necessary to recognise that they use two different processes with different aims and methods (6, 7). NICE produces government funded national guidelines intended for population treatment based on both clinical evidence and cost-effective analysis. NICE start with a series of questions, which can be quite specific, based on feedback from a broad range of stakeholders. ESC and ESH are medical societies who fund the clinical guideline development, with a broad scope, intended for treatment of individuals in many European countries with different socio-economic populations. The societies are largely made up of subject specialists whose needs drive the guidelines. The ESC/ESH guideline therefore encompasses nearly all aspects of blood pressure (BP) control, including for example pregnancy and perioperative management. NICE on the other hand produces a broad range of guidelines and the scope of

each is more focussed in order to reduce overlap between guidelines. As a result, the management of hypertension in pregnancy and management of hypertension for secondary prevention of established cardiovascular disease, or in those with CKD, were excluded from the scope of the hypertension guideline and covered in separate guidelines.

Differences in recommendations within the treatment pathway were in part due to differences in the guideline scopes. The ESC/ESH recommendations for initial single pill combinations were justified by evidence of improved adherence (8, 9). Gupta et al, using urine analysis to indicate the absence of prescribed drugs, demonstrated a linear relationship between the number of pills a patient was expected to take and their lack of adherence (9). This evidence was not included in the NICE guideline due to adherence not being within the scope and instead there is a cross-reference to the NICE Medicines Adherence Guideline (10). Recommendations for resistant hypertension were similar between the guidelines although based on different rationales. The ESC/ESH based recommendations on the PATHWAY-2 study, which found a short-term benefit of spironolactone for blood pressure outcomes (11). NICE instead based recommendations for resistant hypertension on consensus in the absence of evidence. These recommendations were also consistent with the findings of PATHWAY-2, although this trial was excluded from the review due to only having short-term, surrogate outcomes.

The guideline development process also differed between guidelines. The ESC/ESH guideline is based on a 'Task Force' of 21, mostly specialist, physicians who review five classes of graded evidence. The Committee for Practice Guidelines oversees this process. ESC/ESH is very inclusive of all available evidence, including health economics papers, but has no in-house health economics capability. After publication it is the individual 'National Societies' who are responsible for endorsement, translations and implementation.

On the other hand, NICE guidelines involve a slightly smaller committee, representing a diverse composition of knowledge and experience, tailored to each guideline topic. A chair is appointed before scoping who should not have direct reputational or financial conflicts of interest, and is thus usually a non-specialist. The committee includes a mix of people from primary and secondary care as well as patients. A technical team including systematic reviewers and health economists assists the committee and undertakes the systematic reviews rating evidence according to the GRADE process. NICE emphasise the importance of pre-specifying the areas covered within the guideline in order to reduce bias. As a result, the protocols for each systematic review are predefined early in the development process and the committee determine the evidence level that would be required to inform recommendations. The committee also select the areas of the scope that require original health economics analyses, based on where recommendations may have the highest resource impact. NICE guidelines undergo internal quality assurance and a public consultation phase before the final document is published whereas ESC/ESH utilise internal peer review.

The evidence base and its interpretation also differed within each guideline, which had implications for recommendations. This fundamental difference in interpretation is exemplified by the SPRINT trial. NICE considered that the methodology of measuring BP could not be translated into UK clinical practice and so did not lower the recommended treatment target. The use of automated devices set on a time delay, with an unaccompanied rest period, is not common practice in the UK and was considered likely to result in significantly lower BP readings than those taken in routine clinical practice. Other concerns related to the heterogeneity of study populations (inclusion of patients with established cardiovascular or renal disease), and limited long-term safety data at lower achieved blood pressures. The NICE committee therefore could

not confidently recommend a lower BP target for the UK population. However, the NICE guideline acknowledges the possible benefits of lower BP targets and recommendations now emphasise the importance of maintaining BP below 140/90mmHg. ESC/ESH considered the limitations of the BP measurement and made the interpretation that the lower and higher targets in SPRINT would correspond to 130-140mmHg versus 140-150mmHg respectively. Both guideline committees considered the risk of harms of treatment versus the benefits. In both guidelines, recommendations related to targets in the type 2 diabetes population were based on the results of the ACCORD study, which was similar to SPRINT in design but did not show similar benefits of lower targets (12).

Both guidelines made similar recommendations on when to initiate treatment, including all adults with stage 2 or 3 hypertension, as well as people with persistent stage 1 hypertension who have at least moderate ten-year cardiovascular risk. In support of this recommendation, the ESC/ESH guideline cited the results of the HOPE-3 primary prevention study, which showed that treatment for people with stage 1 hypertension and intermediate cardiovascular risk resulted in a significant reduction in major cardiovascular outcomes (13). The NICE guideline was more prescriptive with the specific risk threshold at which to initiate treatment, suggesting this should be based on ten-year cardiovascular risk assessment using a tool such as QRISK2. NICE based this advice on the results of an original health economics model produced for the guideline, incorporating the treatment effects from Brunstrom et al's meta-analysis (14). This found that treatment initiation at a 10% QRISK2 threshold gave an incremental cost-effectiveness ratio (ICER) of £10k for males at age 60 and was therefore deemed cost-effective. Treatment initiation was not strongly recommended below this threshold because the benefit of treatment was less certain, with evidence from observational research that treating low risk stage

hypertension (<10% ten year CVD risk), a group not included in previous RCTs, could result in harm from treatment side-effects(15).

Regarding the elderly and very elderly, both guidelines acknowledge the distinction between frailty and simply advancing age, and take into account the uncertainty around the evidence for treatment effects. However, ESC/ESH conclude that less intensive treatment in the elderly could be too conservative for those who are active and independent rather than frail. NICE decided to retain recommendations for a less intensive initiation threshold and treatment target of 150/90mmHg based on HYVET (16), due to the lack of direct comparative evidence for the influence of frailty in this population. Both NICE and ESC/ ESH recommend the use of standing blood pressure measurements for people with diabetes, symptoms of postural hypotension or age above 80.

There are therefore both similarities and differences between the two guidelines. Both guidelines seek to direct health professionals to the most clinically effective treatments, but some discrepancies exist due to differences in the aims, context and methodologies of each guideline.

## **Disclaimer**

The NICE guideline referred to in this article was produced by the National Guideline Centre for the National Institute for Health and Care Excellence (NICE). The views expressed in this article are those of the authors and not necessarily those of NICE.

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**Table summarising ten specific areas in each hypertension guideline**

	<b>ESC/ESH 2018</b>	<b>NICE 2019</b>
Diagnosis of hypertension using office measurements of blood pressure	$\geq 140/90$ mmHg	$\geq 140/90$ mmHg
Start medication in grade/stage 1 hypertension when;	Lifestyle has failed to control blood pressure and there is low moderate risk	Risk $\geq 10\%$ and lifestyle interventions have failed
Number of drugs used to initiate treatment	Two unless systolic blood pressure is $<150$ mmHG or the patient is frail	One
Single pill combination therapy	Use two or three medication single pills	No recommendation
Office systolic blood pressure target for those aged 18 to 64	$<120 - 129$ mmHg	$<140$ mmHg
Office systolic blood pressure target for those aged 65 to 69	$<130 - 139$ mmHg	$<140$ mmHg
Office systolic blood pressure target for those aged $\geq 80$	$<130 - 139$ mmHg	$<150$ mmHg
Office diastolic blood pressure target	$<80$ mmHg	$<90$ mmHg
Threshold to treat blood	$\geq 140/90$ mmHg	$\geq 140/90$ mmHg

pressure in people with diabetes using office measurements		
Office blood pressure target in people with diabetes	<130/80 mmHg	<140/90 mmHg

### **Authors:**

#### **Terry McCormack**

MBBS MRCA FBIHS FESC

Honorary Reader in Primary Care Medicine

Institute of Clinical and Applied Health Research, Hull York Medical School

Conflicts of interest listed in NICE website

#### **Rebecca Boffa**

BSc(Hons)

Senior Research Fellow

National Guideline Centre, Royal College of Physicians, London, UK

No conflicts of interest.

#### **Nicholas Jones**

MSc MClinEd MRCGP MBBS FHEA

Welcome Trust Doctoral Research Fellow

Nuffield Department of Primary Care Health Sciences, University of Oxford

No conflicts of interest to declare

**Serena Carville**

BSc(Hons) PhD

Associate Director

National Guideline Centre, Royal College of Physicians, London, UK

No conflicts of interest

**Richard J McManus**

MA PhD MBBS FRCGP FRCP

NIHR Research Professor

Nuffield Department of Primary Care Health Sciences, University of Oxford

Conflicts of interest listed on NICE website