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# What is new in hypertension guidelines?

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**ABSTRACT**

In recent years, trials were published and a series of new evidences were presented in relation to hypertension (HT), requiring changes in guidelines. In the light of these studies, the European Society of Hypertension (ESH)/European Society of Cardiology (ESC) HT guideline which was published in 2007 and reviewed in 2009 was revised. The new ESH/ESC HT 2013 guideline announced at the European Hypertension Congress in Milan was published in both Journal of Hypertension and European Heart Journal, and put at the disposal of doctors. In December 2013, the eight Joint National Committee (JNC 8) HT treatment guideline which had been expected for a long time and published online on the Journal of the American Medical Association was issued. Unlike the previous JNC guidelines and ESH/ESC HT guideline, it was a brief guideline containing only recommendations and explaining the grounds of the recommendations. A day before the publication of JNC 8 hypertension treatment guideline, American Society of Hypertension/International Society of Hypertension (ASH/ISH) HT treatment guideline was published. This guideline was also kept short like JNC 8, but contained more details. In this review, we summarized and compared the changes made in the new guidelines.

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## 1. Introduction

Significant changes were made in the European Society of Hypertension (ESH)/European Society of Cardiology (ESC) Hypertension (HT) 2013 guideline (Mancia et al., 2013). For the first time in the guideline, all the data were rated according to ü other guidelines. Unlike the previous Joint National Committee (JNC) guidelines and ESH/ESC HT guideline, JNC 8 (James et al., 2013) is a brief guideline containing only recommendations and explaining the grounds of the recommendations. American Society of Hypertension/ International Society of Hypertension (ASH/ISH) guideline (Weber et al., 2014) was also kept short like JNC 8, but contained more details.

### European Society of Hypertension (ESH)/European Society of Cardiology (ESC) hypertension guideline

The previous ESH/ESC HT classification was not changed (Mancia et al., 2007; Mancia et al., 2013). Blood pressure values were classified as optimum (systolic blood pressure=(SBP)<120 mmHg and diastolic blood pressure=(DBP)<80 mmHg), normal (SBP 120-129 mmHg and/or DBP 80-84 mmHg), high normal (SBP 130-139 mmHg and/or DBP 85-89 mmHg), grade 1 hypertension (SBP 140-159 mmHg and/or DBP 90-99 mmHg), grade 2 hypertension (SBP 160-179 mmHg and/or DBP 100-109 mmHg), grade 3 hypertension (SBP≥180 mmHg and/or DBP≥110 mmHg) and isolated systolic hypertension (SBP≥140 mmHg and DBP<90 mmHg) (Mancia et al., 2013).

Using different types of measurements, minor changes were made in blood pressure (BP) threshold values for the definition of HT; the limits in the previous guidelines were further clarified. Threshold values were defined as SBP≥140 mmHg and/or DBP≥90 mmHg for office BP, SBP≥135 mmHg and/or DBP≥85 mmHg for ambulatory daytime BP, SBP≥120 mmHg and/or DBP≥70 mmHg for ambulatory nighttime BP, SBP≥130 mmHg and/or DBP≥80 mmHg for ambulatory 24

hour BP, and SBP≥135 mmHg and/or DBP≥85 mmHg for home BP (Mancia et al., 2013).

Emphasis was placed on the importance of diagnosing HT and it was recommended that HT diagnosis should be verified with two measurements each time in a patient who was examined no less than twice. It was emphasized that office BP measurement was the gold standard for the screening, diagnosis and treatment of hypertension. Cut-off values for out-of-office BP (ambulatory and home) measurement were 130/80 mmHg, 135/85 mmHg, and 120/70 mmHg for 24 hour ambulatory BP, home and ambulatory daytime BP, and ambulatory nighttime BP, respectively. It was stressed that, for out-of-office BP measurement, major indications were suspicion of white-coat HT, masked or nocturnal HT and hypotensive episodes, and resistance to drug therapy (Mancia et al., 2013).

Starting from 2003 ESH/ESC guideline (Guidelines Committee, 2003), the guidelines pointed out that diagnosis and treatment of HT should be accompanied by measurement of total cardiovascular risk. In other words, diagnosis and treatment should rely on total cardiovascular risk assessment in addition to appropriate BP measurement. Total cardiovascular risk is stratified into four risk categories (low, moderate, high, very high) according to presence or absence of risk factors such as smoking and dyslipidemia; presence or absence of asymptomatic organ damage; diabetes; the stage of chronic kidney disease and symptomatic cardiovascular disease. Some changes were made in the cardiovascular risk chart according to hypertension and risk factor/target organ damage categories. In the new guideline (Mancia et al., 2013), presence of three or more risk factors in the absence of target organ damage was defined as a separate category. Thus, the number of risk factor target organ damage categories were raised from four to five. No risk was assigned any longer to the normal blood pressure category among the blood pressure categories. Therefore, the number of columns was reduced by one (Table 1).

In all hypertensive patients, the target BP level is <140/90 mmHg including low, moderate and high risk groups. In line with the changes to total cardiovascular risk classification, treatment recommendations for the normal blood pressure group were removed. No drug treatment other than a change of lifestyle was recommended for the patients in the high normal class (130-139 mmHg systolic, 85-90 mmHg diastolic) irrespective of the risk factor. For the high or very high risk class, it was recommended that antihypertensive drugs be initiated immediately together with lifestyle measures. For the low and medium risk, it was recommended that antihypertensive therapy be initiated if BP proves to be above 140/90 mmHg after lifestyle changes for a few months or weeks. Drug treatment was not recommended for young patients with high normal BP and isolated systolic hypertension (Mancia et al., 2013).

In ESC/ESH 2013 guideline (Mancia et al., 2013), BP targets were <140 mmHg, save a few exceptions. For elderly hypertensive patients under 80 years of age, HT treatment initiation threshold was ≥160 mm Hg and target systolic blood pressure was 140-150 mmHg. It was emphasized that target SBP value for the elderly patients aged above eighty was 140-150 mm Hg. It was recommended that SBP <140 mmHg could be targeted in the fit elderly under eighty years of age. DBP target was recommended as <90 mmHg except for diabetic patients. DBP target for diabetics was expressed as <85 mmHg.

Special attention is accorded to lifestyle changes in treatment, and salt reduction, regular appropriate exercise, weight control, reduction of alcohol intake, giving up smoking, and diet are recommended. Where salt reduction is concerned, the previous guideline (Mancia et al., 2007) recommends <5 grams, while the new guideline (Mancia et al., 2013) recommends between 5-6 grams.

It was stated that the real benefit of hypertensive treatment was due to the fall in BP and therefore all the drugs in the five main classes [thiazide-type diuretics, calcium channel blockers (CCB), angiotensin-converting-enzyme-inhibitors (ACEI), angiotensin receptor blockers (ARB) and beta blockers] could be used as a mono-therapy or a combination therapy in any sequence when initiating the treatment (Mancia et al., 2013). Appropriate combinations of these drugs other than ACEI + ARB combination and beta blockers are recommended. Combination therapy was recommended to be initiated immediately in high risk patients and Grade

**Table 1.** Comparison of total cardiovascular risk in different hypertension guidelines

| Other risk factors, asymptomatic organ damage or disease | | Blood pressure | | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|
| | | Normal | | High normal | | Grade 1 HT | | Grade 2 HT | | Grade 3 HT | |
| ESH/ESC 2007 HT guidelines | ESH/ESC 2013 HT guidelines | 2007 | 2013 | 2007 | 2013 | 2007 | 2013 | 2007 | 2013 | 2007 | 2013 |
| No other RF | No other RF | Average risk | | Average risk | | Low added risk | Low risk | Moderate added risk | Moderate risk | High added risk | High risk |
| 1-2 RF | 1-2 RF | Low added risk | | Low added risk | Low risk | Moderate added risk | Moderate risk | Moderate added risk | Moderate to high risk | Very high added risk | High risk |
| ≥3 RF, MS, OD or Diabetes | ≥3 RF | Moderate added risk | | High added risk | Low to moderate risk | High added risk | Moderate to high risk | High added risk | High risk | Very high added risk | High risk |
| Established CVOD, CKD stage 3 or renal disease | diabetes | Very high added risk | | Very high added risk | Moderate to high risk | Very high added risk | High risk | Very high added risk | High risk | Very high added risk | High to very high risk |
| | Symptomatic CVD, CKD stage ≥4 or diabetes with OD/RFs | | | | Very high risk | | Very high risk | | Very high risk | | Very high risk |

**CKD**: Chronic kidney disease; **CVD**: Cardiovascular disease; **OD:** Organ damage; **RF**: Risk factor; **MS**: Metabolic syndrome; **HT**: Hypertension; Adapted from European Society of Hypertension (ESH)/ European Society of Cardiology (ESC) hypertension 2013 and ESH/ESC hypertension 2007 guidelines.

2 and 3 patients. It was reported that combination therapy induced faster response, less side effects, better tolerance, higher physiological and pharmacological synergy, higher possibility to reach the target blood pressure, and higher patient adherence, and if applicable, administration of a fixed dose with a single tablet was recommended. In addition, the therapy was recommended to be initiated with an optimal dose, i.e. full dose (Mancia et al., 2013).

A minor change was made in the section dealing with antihypertensive therapies, which should be preferred in special cases. While only calcium antagonist was recommended for the peripheral arterial disease in the previous guideline (Mancia et al., 2007). ACEI was added to calcium antagonist in the new guideline (Mancia et al., 2013). Aortic aneurysm was also included as a manifestation, wherefore the use of a beta blocker was proposed (Mancia et al., 2013). In the previous guideline (Mancia et al., 2007) atrial fibrillation classified recurrent and permanent categories, and an ARB or ACEI was recommended for the former, and a beta blocker or a non-dihydropridin calcium antagonist was recommended for the latter. In the new guideline atrial fibrillation treatment was split into prevention and ventricular ratecontrol categories; an ARB, ACEI, beta-blocker or mineralocorticoid receptor antagonist was recommended for the former, whereas a beta blocker or a non-dihydropridin calcium antagonist was recommended for the latter. While the previous guideline recommended ACEI, ARB, and loop diuretic for end-stage kidney disease/proteinuria, the new guideline removed loop diuretic (Mancia et al., 2007; Mancia et al., 2013).

In ESC/ESH 2013 guideline (Mancia et al., 2013) BP target for diabetics was <140/85 mmHg. In the presence of microalbuminuria and proteinuria, renin-angiotensin system (RAS) blockers should be preferred as they are more effective in reducing proteinuria than other antihypertensive agents, but dual blockage of RAS should be avoided (Mancia et al., 2013). In the presence of nephropathy, initiation of the drug was recommended if SBP≥140 mmHg. Target SBP is <140 mmHg. While the target was 120/80 mmHg for overt proteinuria in the previous guideline, SBP<130 mmHg was recommended in the new guideline. Aldosterone receptor antagonist was not recommended in chronic kidney disease especially in combination with a RAS blocker because of the risk of excessive reduction in renal function and of hyperkalemia (Mancia et al., 2013).

In ESC/ESH 2013 guideline (Mancia et al., 2013), resistant HT was defined as HT that cannot be controlled with a treatment strategy that includes appropriate lifestyle measures plus minimum three drugs, including a diuretic. In resistant individuals, it was recommended to include mineralocorticoid receptor antagonist, amiloride and/or alpha 1 blocker doxazosin in the treatment strategy. If drug therapy fails, invasive procedures such as renal denervation (denervation of renal sympathetic nerves with radio frequency ablation) or baroreceptor stimulation (a baroreceptor activation device comprised of an implantable pulse generator that can activate the carotid sinus with electric signals) were recommended. However, it was stated that further procedures were required to be performed at experienced centers since these procedures were yet at investigation stage and results were insufficient (Mancia et al., 2013).

There were minor changes in the recommendation of drug therapy in pregnancy. In the previous guideline (Mancia et al., 2007), the BP levels for the initiation of drug treatment were SBP ≥150 mmHg or DBP ≥95 mmHg for pregnants and >140/90 mmHg for gestational HT (with or without proteinuria). SBP≥170 mmHg or DBP≥110 mmHg were regarded as emergency cases that require urgent hospitalization (Mancia et al., 2007). In the new guideline class I drug treatment for SBP>160 mmHg or DBP>110 mmHg was recommended. For SBP≥150 mmHg or DBP ≥95 mmHg, it was stated that drug treatment (Class IIb) may be considered. Similar to the previous guideline, the threshold value for drug treatment was 140/90 mmHg for women with gestational HT (with or without proteinuria), preexisting hypertension with the superimposition of gestational hypertension or hypertension with asymptomatic organ damage or symptoms at any time during pregnancy. Metildopa, labetalol and nifedipine are the recommended antihypertensive agents. Intravenous labetolol and nitroprusside infusion are recommended as preferable antihypertensive agents in emergency cases (preeclampsia) (Mancia et al., 2013).

While BP target in the previous guideline was 130/80 mmHg for hypertensive patients with a history of stroke and transient ischemic attack, the target was lowered below 140 mmHg in the new guideline. No treatment strategy to lower BP is recommended in the first week after acute stroke. Similarly, in coronary heart disease, antihypertensive treatment was recommended to be initiated for SBP>140 mmHg, and target SBP was assigned as <140 mmHg (Mancia et al., 2007; Mancia et al., 2013).

**Joint National Committee (JNC) 8 and American Society of Hypertension/International Society of Hypertension (ASH/ISH) hypertension guidelines**

Unlike the previous JNC guidelines and ESH/ESC HT guideline, JNC 8 (James et al., 2013) is a brief guideline containing only recommendations and explaining the grounds of the recommendations. JNC 7 (Chobanian et al., 2003) published in 2003 was about 47 pages whereas JNC 8 is a guideline of 14 pages. The authors presented 9 recommendations substantiated by strong evidences. Randomized controlled trials (RCTs) were taken as the gold standard for the evidences. JNC 7 defined prehypertension, whereas the new guideline defined threshold values for pharmacological treatment (Chobanian et al., 2003; James et al., 2013) JNC 7 addressed several issues such as blood pressure methods, secondary hypertension, resistant hypertension, and HT in a special population based on expert opinions and literature reviews (Chobanian et al., 2003). The new guideline assessed a limited number of issues because RCTs were given higher priority (James et al., 2013).

**Recommendation 1** (James et al., 2013): In the general population aged < 60 years, target BP should be below 150/90 mmHg. Pharmacologic treatment should be initiated in BP ≥150/90 (Strong Recommendation, Grade A). In this age group, there is no need to change treatment if the treatment is well tolerated and there are no side effects even if SBP falls below the target values (for example <140 mmHg) (Expert Opinion-Grade E).

**Recommendation 2** (James et al., 2013): In the general population aged <60 years, the target should be DBP <90 mmHg and treatment should be initiated above this value

(For ages 30-59, Strong Recommendation Grade A; For ages 18-29, Expert Opinion-Grade E). This recommendation depends on 5 DBP trials conducted on hypertensive patients between 30-69 years of age (Effects of treatment on morbidity in hypertension, II: Results in patients with diastolic blood pressure averaging 90 through 114 mmHg, 1970; Hypertension-Stroke Cooperative Study Group, 1974; Hypertension Detection and Follow-up Program Cooperative Group, 1979; Report by the Management Committee, 1980; Hypertension Detection and Follow-up Program Cooperative Group, 1982; Medical Research Council Working Party, 1985). The reason why the recommendation remains as an expert opinion for individuals <30 years is lack of sufficient RCT on this issue.

**Recommendation 3** (James et al., 2013): In patients aged <60 years, the threshold to initiate treatment is SBP≥140 mmHg. Target SBP<140 mm Hg (Expert Opinion-Grade E)

**Recommendation 4** (James et al., 2013): In patients aged >18 years with chronic kidney disease (CKD), treatment should be initiated at SBP≥140 or DBP≥90 mmHg. The treatment target is <140/90 mmHg (Expert Opinion-Grade E)

**Recommendation 5** (James et al., 2013): In patients aged ≥18 years with diabetes, treatment should start at SBP ≥140 mmHg or DBP ≥90 mmHg. The treatment target is <140/90 mmHg (Expert Opinion-Grade E).

In JNC 7, the target BP was <130/80 mmHg for patients with diabetes or chronic kidney disease (Chobanian et al., 2003). ACCORD trial was a study that investigated the effect of intensive BP control on cardiovascular events in diabetic patients with high cardiovascular risk (Cushman et al., 2010). According to the results of ACCORD-BP trial, no difference was identified in diabetic patients in terms of primary end-points (cardiovascular death, non-fatal stroke, myocardial infarction) between a strategy that targeted a SBP of <120 mmHg and a strategy that targeted a SBP<140 mmHg (Cushman et al., 2010). The panel made this recommendation as a result of these data.

**Recommendation 6** (James et al., 2013): In the general non-black population, including those with diabetes, initial hypertensive treatment should include a thiazide-type diuretic, CCB, ACEI or ARB (Moderate Recommendation-Grade B). Since higher primary endpoints (cardiovascular mortality, myocardial infarction and stroke) were seen in beta-blockers in a randomized controlled trial (LIFE) making a comparison with ARB, beta blockers were not recommended as the choice of initial treatment.

In ALLHAT trial (Antihypertensive and Lipid-Lowering Treatment to Prevent Heart Attack Trial Colaborative Research Group, 2003), alpha blockers were not recommended as the choice of initial treatment as they exhibited worse cardiovascular outcome compared with diuretic treatment.

Due to lack of sufficient RCTs of appropriate quality, the use of carvedilol, nebivolol, clonidine, hydralazine, spironolactone, reserpine and furosemide were not recommended as an initial treatment. Due to lack of sufficient RCTs of appropriate quality, dual $\alpha_1\beta$-blocker agents (carvedilol), vasodilator $\beta$-blockers (nebivolol), central $\alpha_2$–adrenergic agonists (clonidine), direct vasodilators (hydralazine), aldosteron receptor antagonists (spironolactone), peripheral-acting adrenergic antagonists (reserpine) and loop diuretics (e.g. furosemide) were not recommended as first-line treatment (James et al., 2013).

**Recommendation 7** (James et al., 2013): In the general black population, including those with diabetes, initial antihypertensive treatment should include thiazide-type diuretic or CCB. (For general black population: Moderate Recommendation-Grade B; for black patients with diabetes: Weak Recommendation-Grade C).

**Recommendation 8** (James et al., 2013): In the population aged ≥18 with chronic kidney disease (CKD), initial or add-on antihypertensive treatment should include an ACEI or ARB to improve kidney outcomes (Moderate Recommendation-Grade B). This recommendation applies to all chronic kidney patients, independently of race and diabetic condition.

**Recommendation 9** (James et al., 2013): The primary purpose of HT treatment is to reach and maintain target blood pressure. If BP treatment target has not been reached in the first month, the dose of the initial drug should be increased or a second drug added. The add-on drug should be one of the drugs listed in Recommendation 6 (Thiazide, CCB, ACEI or ARB). If target blood pressure cannot be reached with two drugs after a reasonable period of time, a third drug should be considered. ACEI and ARB should not be used together. If target blood pressure cannot be reached using the drugs in recommendation 6 because of a contraindication or the need to use more than three drugs, antihypertensive drugs from other classes can be used. Referring complicated patients with whom the target blood pressure cannot be reached using the above strategy and who require additional clinical consultation to a hypertension specialist may be indicated (Expert Opinion-Grade E).

When the results of ALLHAT trial (Antihypertensiveand Lipid-Lowering Treatment to Prevent Heart Attack Trial Collaborative Research Group, 2003) showed that thiazide diuretics were effective drugs in BP control as a first-line and combination treatment, JNC 7 guideline recommended the use of diuretics in the first-line therapy (Chobanian et al., 2003). Although five drug classes were suitable for initial treatment in JNC 7, thiazide diuretics were recommended as initial treatment unless there were indications requiring the use of another class (Chobanian et al., 2003). JNC 8 stated that any one of thiazide diuretic, CCB, ACEI or ARB could be used as initial treatment. Beta blocker was not included in the drugs of first choice unlike ESH/ESC and JNC 7. In diabetic patients and patients with CKD, treatment initiation threshold and the target blood pressure to be reached were revised as 140/90 mmHg. In JNC 7 guideline (Chobanian et al., 2003), the recommended level was 130/80 mmHg for these patients. First of all, treatment initiation threshold was revised as ≥150/90 mmHg and target blood pressure as <150/90 mmHg for patients aged 60 and above (James et al., 2013). These figures were ≥140/90 mmHg and <140/90 mmHg, respectively, in JNC 7 (Chobanian et al., 2003).

In JNC 8, instead of the word “elderly”, a clear statement such as ≥60 years was included. However, 150 mmHg was accepted instead of 160 mm Hg in ESH/ESC (James et al., 2013; Mancia et al., 2013). While ESC/ESH retained beta blockers among the primary drug group to be preferred first, JNC 8 excluded beta blockers (James et al., 2013; Mancia et al., 2013). ESC/ESH revised target blood pressure to 140/85 mmHg in patients with diabetes and patients with kidney dysfunction, and recommended a systolic blood pressure of

<130 mmHg for overt proteinuria. JNC 8 suggested 140/90 mmHg as a target for patients with diabetes and CKD. It did not make a special emphasis on overt proteinuria. Both guidelines recommended to avoid combined use of ACEIs ve ARBs (James et al., 2013; Mancia et al., 2013).

Some confusing differences are noted in JNC 8 (James et al., 2013) and American Society of Hypertension/International Society of Hypertension (ASH/ISH) (Weber et al., 2014). While the same target BP of <140/90 is recommended for DM and CKD patients, there are differences in other aspects (James et al., 2013; Weber et al., 2014). The initial treatment threshold value, i.e. 150/90 mmHg which applies to patients aged 60 and above in JNC 8 applies to patients aged 80 and above in ASH/ISH guideline (James et al., 2013; Weber et al., 2014). In ASH/ISH guideline, ≥140/90 mmHg was recommended for the diagnosis of HT in adult patients under 80 years of age. ASH/ISH guideline recommends different drugs than those recommended by JNC 8 as initial treatment subject to race, age and blood pressure level of patients. While JNC 8 states an ACEI, ARB, CCB or thiazide diuretic as the initial choice for the white race, ASH/ISH guideline recommends an ACEI or ARB for the white race under 60 years of age and a CCB or thiazide for the white race aged 60 and above. Similar to JNC 8, CCB or thiazide is recommended for the black population. (James et al., 2013; Weber et al., 2014). In HT classification, the definitions of prehypertension (SBP 120-139 and/or DBP 80-89 mmHg), stage 1 (SBP 140-159 mmHg and/or DBP 90-99 mmHg ) and stage 2 (SBP≥160 mmHg and/or DBP≥100) which were given in JNC 7 were preserved (Chobanian et al., 2007; James et al., 2013; Weber et al., 2014).

**Table 2.** Hypertension guidelines comparisons of goal blood pressure and initial drug therapy

| Guideline | Population | Goal BP,mmHg | Initial drug treatment options |
|---|---|---|---|
| **JNC 8** | aged≥60 | <150/90 | |
| | aged<60 | <140/90 | |
| | Diabetes | <140/90 | |
| | CKD | <140/90 | |
| **ESH/ESC 2013** | nonelderly | <140/90 | ACEI, ARB, β-Blocker,diuretic or CCB |
| | elderly aged<80y | <150/90 | |
| | aged ≥80 y | <150/90 | |
| | Diabetes | <140/85 | ACEI or ARB |
| | CKD no proteinuria | <140/90 | ACEI or ARB |
| | CKD+proteinuria | <130/90 | |
| **ASH/ISH** | aged ≥80 | <150/90 | White and other non-black patients: Aged <60 ACEI or ARB, White and other non-black patients: Aged >60 years CCB or thiazide-type diüretic, black patients all ages CCB or thiazide-type diüretic |
| | aged<80 | <140/90 | |
| | Diabetes | <140/90 | ARB or ACE inhibitor Note: in black patients, it is acceptable to start with CCB or thiazide |
| | CKD | <140/90 | ARB or ACE inhibitor Note: in black patients, good evidence for renal protective effects of ACE inhibitors |

*__ESH:__ European Society of Hypertension; **ESC**: European Society of Cardiology; **JNC:** Joint National Committee; **ASH**: American Society of Hypertension; **ISH**: International Society of Hypertension; **CKD**: Chronic kıdney disease; **ACE**: Angiotensin-converting enzyme; **ARB**: Angiotensin receptor blocker; **CCB**: Calcium channel blocker.

## 2. Conclusion

In this review, the changes in new hypertension guidelines were summarized and compared. Significant differences between the guidelines with respect to blood pressure values that may be used to define hypertension and that may be targeted are summarized in Table 2.

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