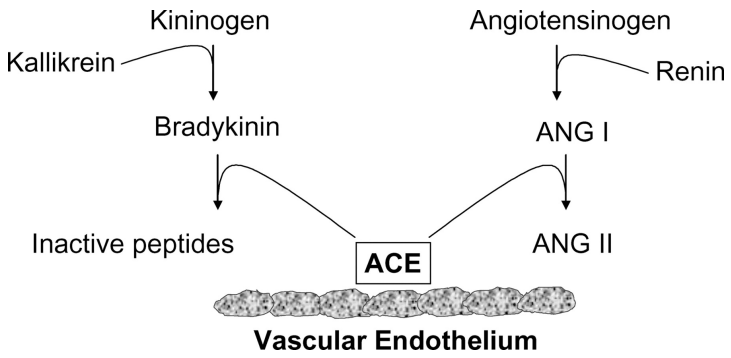
SNP SUMMARY: ANGIOTENSIN 1 CONVERTING ENZYME (ACE) INSERTION/DELETION

Overview	Salt sensitivity is estimated to be present in 51% of hypertensive and 26% of normotensive populations. The Angiotensin 1 converting enzyme (ACE) gene codes for the ACE and is part of the renin-angiotensin system (RAS), which controls blood pressure by regulating fluid volume in the body. The ACE gene variant contributes to salt sensitivity.
Name of gene	Angiotensin 1 converting enzyme (ACE) gene
Symbol of gene	ACE
Gene database	http://www.genecards.org/cgi-bin/carddisp.pl?gene=ACE&search=7b55fd83b2237ace61a214ca0325b4ea
rs number	rs4646994
Base change	The presence or absence (insertion or deletion) of the enzyme is based on a 287 bp Alu repeat element in the gene.
SNP's nomenclature	ACE Insertion/Deletion (I/D)
Name of enzyme	Angiotensin 1 converting enzyme
Nutrient cofactor	Zinc

Population Frequency	Non-Hispanic whites: DD=28.8%, ID=51%, II=19.6% Non-Hispanic black: DD=33.8%, ID=49.8%, II=16.4% Mexican American: DD=20.7%, ID=51.9%, II=27.4%
Impact of SNP on biological pathway/s	• The ACE gene encodes an enzyme involved in catalysing the conversion of angiotensin I into a physiologically active peptide angiotensin II. • Angiotensin II is a potent vasopressor and aldosterone-stimulating peptide that controls blood pressure and fluid-electrolyte balance. • This enzyme plays a key role in the RAS. • Levels of circulating enzyme are associated with the presence or absence of the (rs4646994) 287 bp Alu repeat in this gene.
Biochemical pathway	Schematic diagram of the RAS and kallikrein–kinin system. Angiotensin-converting enzyme is strategically poised to regulate the balance between Ang II and bradykinin.

	Schematic diagram of the renin–angiotensin system and kallikrein–kinin system.  Jeffrey S. Borer Eur Heart J Suppl 2007;9:E2-E9 EUROPEAN HEART JOURNAL SUPPLEMENTS
Nutrient interaction	• Higher salt intakes have a direct effect on blood pressure levels in salt-sensitive individuals, however genotype effects are not likely to be observed in populations consuming low-salt diets. • In addition it is suggested that some factors including age and weight status may play a critical role in how rapidly and how sustained a genotype-specific sodium effect may be.
Established diet-gene interactions	• Meneton et al. (2005) found that the prevalence of salt sensitive hypertension in those with the II genotype and ID genotype was significantly higher than DD genotype. • Zhang et al. (2006) found that in individuals with the ID+II genotype, hypertension was increased by a high salt intake, while in the DD genotype it was not. The interaction was more prominent in the overweight group than in the non-overweight group. • Poch et al. (2001) found that ACE II or ID genotypes had greater increases in blood pressure with high salt intake

<table>
<tr><td></td><td colspan="2">than those homozygous for the deletion allele (DD).</td></tr>
<tr><td>Potential dietary recommendations</td><td colspan="2">The American Heart Association recommends that individuals with high blood pressure ideally:
Aim to eat no more than 2,300 milligrams (approximately 1 level teaspoon of salt) of sodium per day. This may assist in lowering blood pressure. However, reducing daily sodium intake to approximately 1,500 mg is more desirable because it can lower blood pressure even further.
Dietary recommendations:
It is useful to establish whether an individual is salt sensitive or not, as the use of salt in the diet increases palatability, and unnecessary sodium restriction should be avoided.
If sodium restriction is indicated:
Choose and prepare foods with little or no salt, including salt-containing spices, rather flavour with fresh herbs or low-sodium seasonings.
Avoid the addition of extra salt or salt-containing spices at the table e.g. garlic salt.
Limit the intake of high-sodium containing foods e.g. Convenience foods, processed foods, pizza, and dry-packaged foods, mixes, sauces, and soups.
Limit the intake of foods with a naturally high-sodium content e.g. olives, cheese, seafood, and some canned legumes.
Use fresh foods instead of canned and processed foods.
Choose unsalted food products e.g. raw nuts and seeds.
Pay attention to nutritional labelling, the sodium content will be indicated. Low sodium foods are those with less than 120mg of sodium per 100g of food.</td></tr>
<tr><td rowspan="3">Examples of medium to high-sodium containing foods</td><td>Food</td><td>Sodium content per 100g</td></tr>
<tr><td>Canned cream of chicken soup</td><td>460 (medium)</td></tr>
<tr><td>Tomato sauce</td><td>615 (high)</td></tr>
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	Pizza, mixed toppings	640 (high)
	Potatoe chips	670 (high)
	Salami	1850 (high)
	Yeast extract spread e.g Bovril	3300 (high)
References	• Armando, I., Villar, V., & Jose, P. (2015). Genomics and pharmacogenomics of salt-sensitive hypertension. *Current hypertension reviews*. • Hunt, S. C., Cook, N. R., Oberman, A., Cutler, J. A., Hennekens, C. H., Allender, P. S., . . . Williams, R. R. (1998). Angiotensinogen genotype, sodium reduction, weight loss, and prevention of hypertension: trials of hypertension prevention, phase II. *Hypertension, 32*(3), 393-401. • Meneton, P., Jeunemaitre, X., de Wardener, H. E., & Macgregor, G. A. (2005). Links between dietary salt intake, renal salt handling, blood pressure, and cardiovascular diseases. *Physiological Reviews, 85*(2), 679-715. • Norat, T., Bowman, R., Luben, R., Welch, A., Khaw, K. T., Wareham, N., & Bingham, S. (2008). Blood pressure and interactions between the angiotensin polymorphism AGT M235T and sodium intake: a cross-sectional population study. *Am J Clin Nutr, 88*(2), 392-397. • Poch, E., González, D., Giner, V., Bragulat, E., Coca, A., & de la Sierra, A. (2001). Molecular basis of salt sensitivity in human hypertension evaluation of renin-angiotensin-aldosterone system gene polymorphisms. *Hypertension, 38*(5), 1204-1209. • Zhang, L., Miyaki, K., Araki, J., Song, Y., Kimura, T., Omae, K., & Muramatsu, M. (2006). Interaction of angiotensin i–converting enzyme insertion-deletion polymorphism and daily salt intake influences hypertension in Japanese men. *Hypertension research, 29*(10), 751-758. • http://www.nutritionfoundation.org.nz/nutrition-facts/minerals/sodium • http://www.heart.org/HEARTORG/GettingHealthy/NutritionCenter/HealthyDietGoals/Sodium-Salt-or-Sodium-Chloride_UCM_303290_Article.jsp	