



Traitement antihypertenseur et grossesse

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Septembre 2024

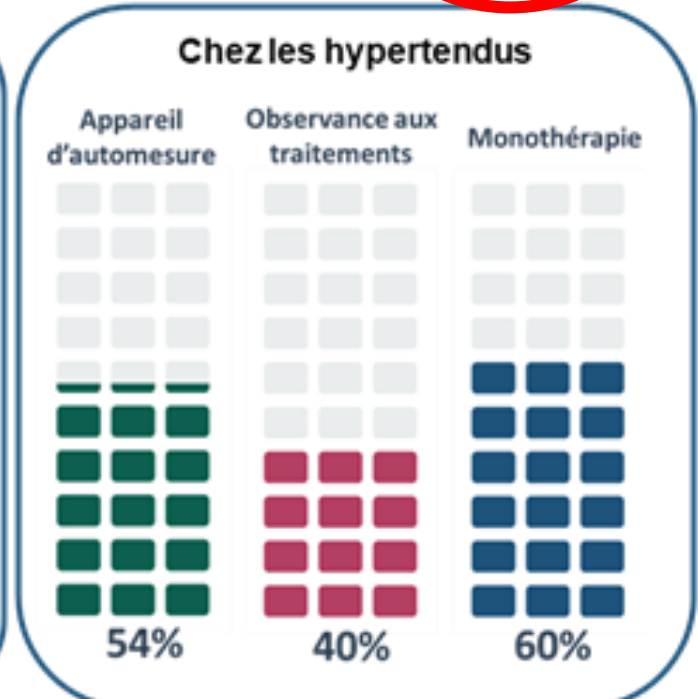
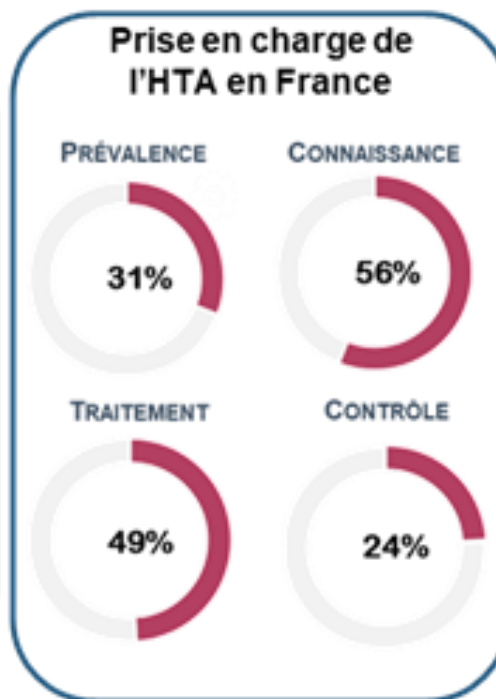
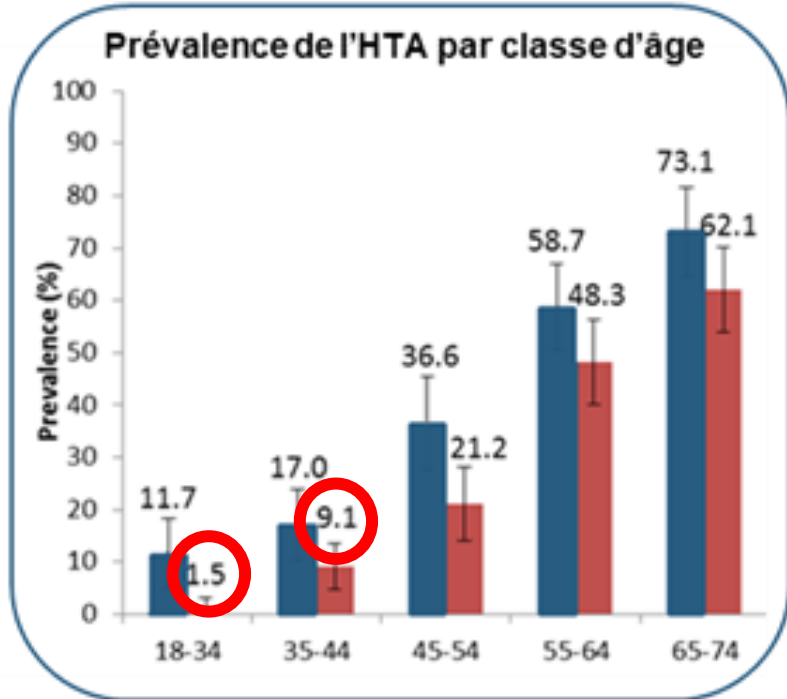
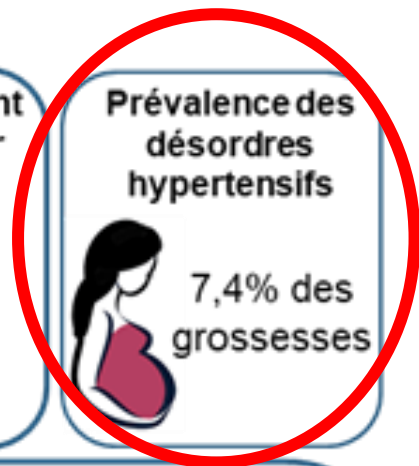
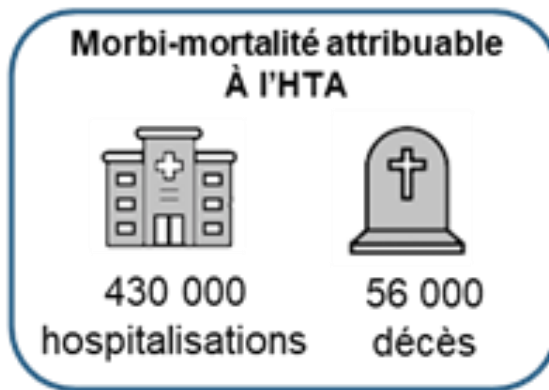
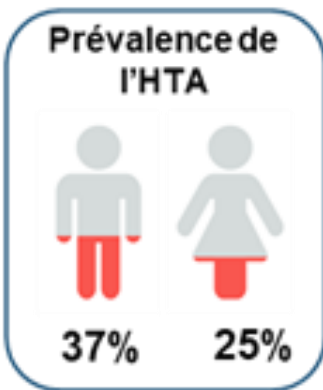


Déclaration de liens d'intérêt de Jacques Blacher :

- Absence de participation financière dans le capital d'une entreprise liée aux médicaments.

- Interventions ponctuelles en rapport avec des entreprises liées aux médicaments (essais cliniques, travaux scientifiques, conseils, comités scientifiques, rapports d'expertise, conférences, colloques, actions de formation, participation à divers symposia, rédaction de brochures...) avec, le cas échéant, facturation d'honoraires ; et ceci avec la majorité des entreprises du médicaments commercialisant des produits cardiovasculaires et autres produits en rapport avec mes domaines de spécialité (Astra-Zeneca, Bayer, ElKendi, Hikma, Icomed, Leurquin, Omron, Organon, Quantum Genomics, Sanofi Aventis, Saint Jude, ViiV, Vivactis, Vivoptim)

- HAS, ANSM, CNAM, MGEN, Santé Publique France



Désordres hypertensifs de la grossesse (DHG)

- 3 entités
 - HTA chronique avant la grossesse
 - Hypertension gravidique
 - Pré-éclampsie
- Problématiques
 - 7.4% des grossesses en France
 - Cause importante de morbi-mortalité :
 - Foétale (Prématurité, Mort foétale, Hématome rétro-placentaire)
 - Maternelle (éclampsie, HELLP syndrome, décès)
 - Risque CV à long terme
 - Hypertension, diabète
 - Maladies cardiovasculaires
 - Décès



La cohorte conception (1)

- SNDS
 - Base de données médico-administrative de l'assurance maladie
 - Toutes les données concernant :
 - Les **hospitalisations** (dates, codes diagnostics...)
 - Les **prestations de ville** :
 - Médicaments
 - Consultations
 - Biologie
 - Imagerie
 - ...



La cohorte conception (2)

- Cohorte conception
 - Tous les accouchements entre 2010 et 2018
 - Naissances à l'hôpital après 22 SA
 - 6,3 millions accouchements
 - 2,9 millions de femmes
 - Suivi jusqu'à 2022





HTA ET GROSSESSE

Consensus d'Experts de la Société Française d'Hypertension Artérielle* (SFHTA)

**SFHTA filiale de la Société Française de Cardiologie*



Société Française
d'Hypertension Artérielle

GROUPE DE TRAVAIL

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Jacques BLACHER (Cardiologue)

www.sfhta.org

RECOMMANDATION 3 - (Grade A - Classe 1)

Il est recommandé de traiter sans délai toutes les hypertensions artérielles sévères (PAS \geq 160 mm Hg ou PAD \geq 110 mm Hg).

RECOMMANDATION 4 - (Grade C - Classe 2)

En cas d'HTA légère à modérée en consultation (PAS = 140-159 mm Hg ou PAD = 90-109 mm Hg), confirmée par l'AMT ou la moyenne diurne de la MAPA (PAS \geq 135 ou PAD \geq 85 mm Hg), la présence d'antécédent cardio-vasculaire, de diabète pré-gestationnel, de maladie rénale chronique ou d'un niveau de risque cardio-vasculaire élevé en prévention primaire, suggère l'initiation d'un traitement antihypertenseur.

RECOMMANDATION 6 - (Grade B - Classe 2)

Pendant la grossesse, il est suggéré d'utiliser en première intention, au choix, l'un des traitements antihypertenseurs suivants (classés par ordre alphabétique) :

l'alpha-méthylidopa, le labétalol, la nicardipine, la nifédipine.

RECOMMANDATION 7 - (Grade A - Classe 1)

Les inhibiteurs de l'enzyme de conversion, les antagonistes des récepteurs de l'angiotensine II et l'aliskiren ne doivent pas être utilisés quel que soit le trimestre de la grossesse et sont contre-indiqués au 2^e et 3^e trimestres de grossesse.

5.1.6. Managing mild hypertension in pregnancy (office blood pressure of 140–159/90–109 mmHg)

Women with pre-existing hypertension on BP-lowering drugs may continue their BP-lowering medication, but RAS inhibitors and most thiazide diuretics are contraindicated during pregnancy and not recommended due to adverse foetal and neonatal outcomes.

The BP-lowering drugs of choice are: beta-blockers (most data available for labetalol, a non-selective beta-blocker that also acts as an alpha-blocker in higher doses; metoprolol and bisoprolol are also considered safe), CCBs (most data available for nifedipine, also felodipine, nitrendipine, amlodipine, and isradipine can be used), and methyldopa.^{386,387} A meta-analysis suggests that beta-blockers and CCBs are more effective than methyldopa in preventing severe hypertension.³⁸⁵ Of note, however, ~~atenolol~~ should be avoided, as it is associated with foetal growth restriction.^{388,389} It should also be highlighted that methyldopa has been associated with increased risk of post-partum depression and caution is therefore advised, both intra-partum and post-partum.³⁹⁰ A large trial is currently evaluating labetalol vs. nifedipine in hypertension of pregnancy (ISRCTN87208603).

5.1.5. Treatment initiation and blood pressure targets

Severe maternal hypertension is a risk factor for adverse maternal and perinatal outcomes,³⁸¹ including ante- and post-partum stroke.³⁸² In the Cardiovascular Health Awareness Program (CHAP) trial, treating pregnant women with chronic hypertension and BP of $\geq 140/90$ mmHg reduced the occurrence of pre-eclampsia with severe features and also reduced medically indicated pre-term birth at <35 weeks; compared with only treating severe hypertension (BP $\geq 160/105$ mmHg).³⁸³ There was no evidence of an increased risk of severe neonatal complications in the intensive treatment group, including small-for-gestational-age birth weight.³⁸³ Of note, the mean BP between randomization and delivery in this trial was 129/79 mmHg in the intensive-treatment arm and 133/82 mmHg in the conservative arm.³⁸³ In another trial, tight BP control (target diastolic BP < 85 mmHg) compared with less-tight

BP control (target diastolic BP < 100 mmHg) improved the incidence of subsequent severe maternal hypertension (BP $\geq 160/110$ mmHg), but not foetal or other maternal outcomes in women with mild hypertension at baseline (diastolic BP of 85–105 mmHg).³⁸⁴

Nonetheless, based on the CHAP trial³⁸³ and a meta-analysis,³⁸⁵ treatment with BP-lowering drugs in all pregnant women with confirmed BP of $\geq 140/90$ mmHg is recommended to reduce the progression to severe hypertension and the related risks for adverse pregnancy outcomes. Therefore, in women with pre-existing and gestational hypertension with and without pre-eclampsia, we recommend lowering BP to below 140 mmHg for systolic and between 80 and 90 mmHg for diastolic BP.³⁸⁴

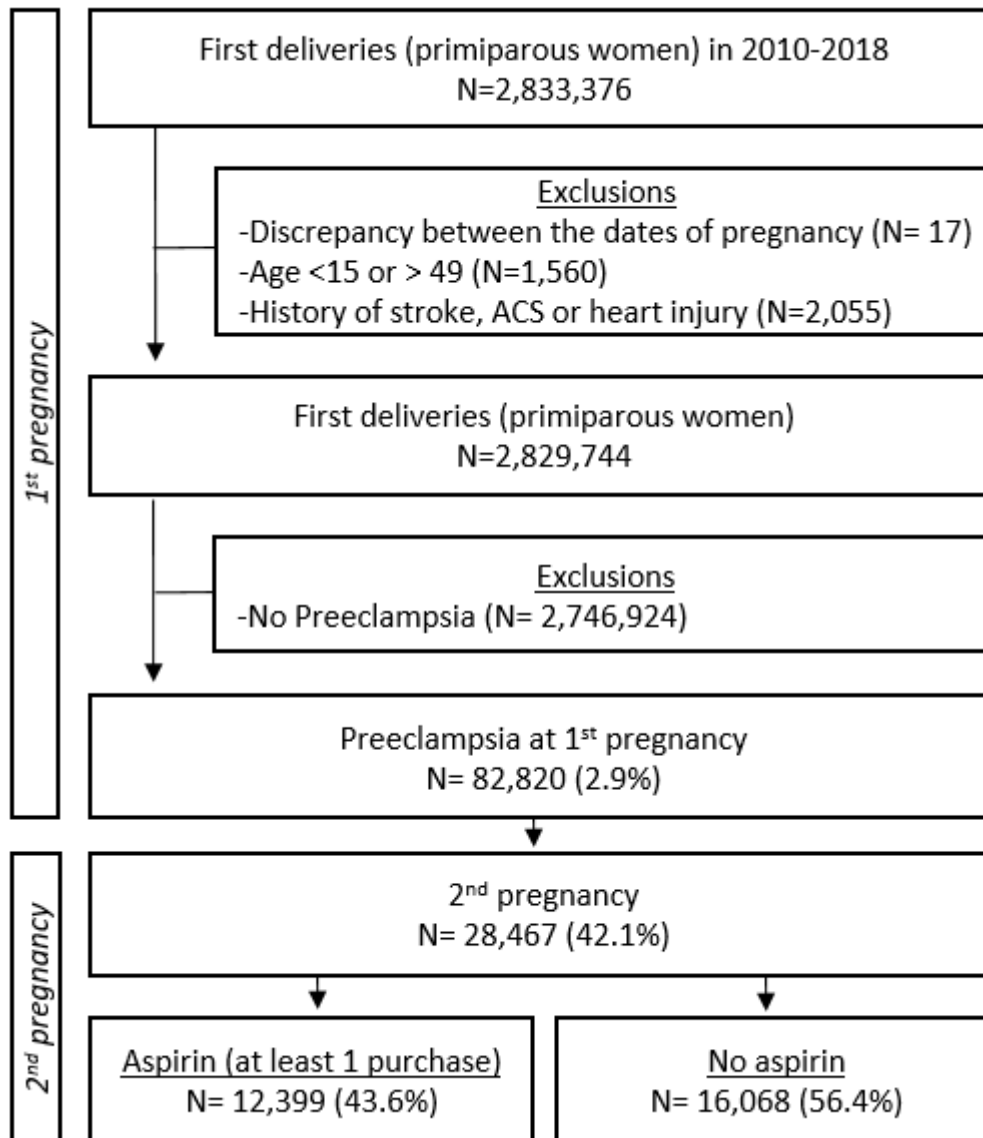
Treatment with BP-lowering drugs in all pregnant women with confirmed BP of $\geq 140/90$ mmHg is recommended to reduce the progression to severe hypertension and the related risks for adverse pregnancy outcomes

Table S11 Blood pressure-lowering medications that are considered safe with breastfeeding^{367,390}

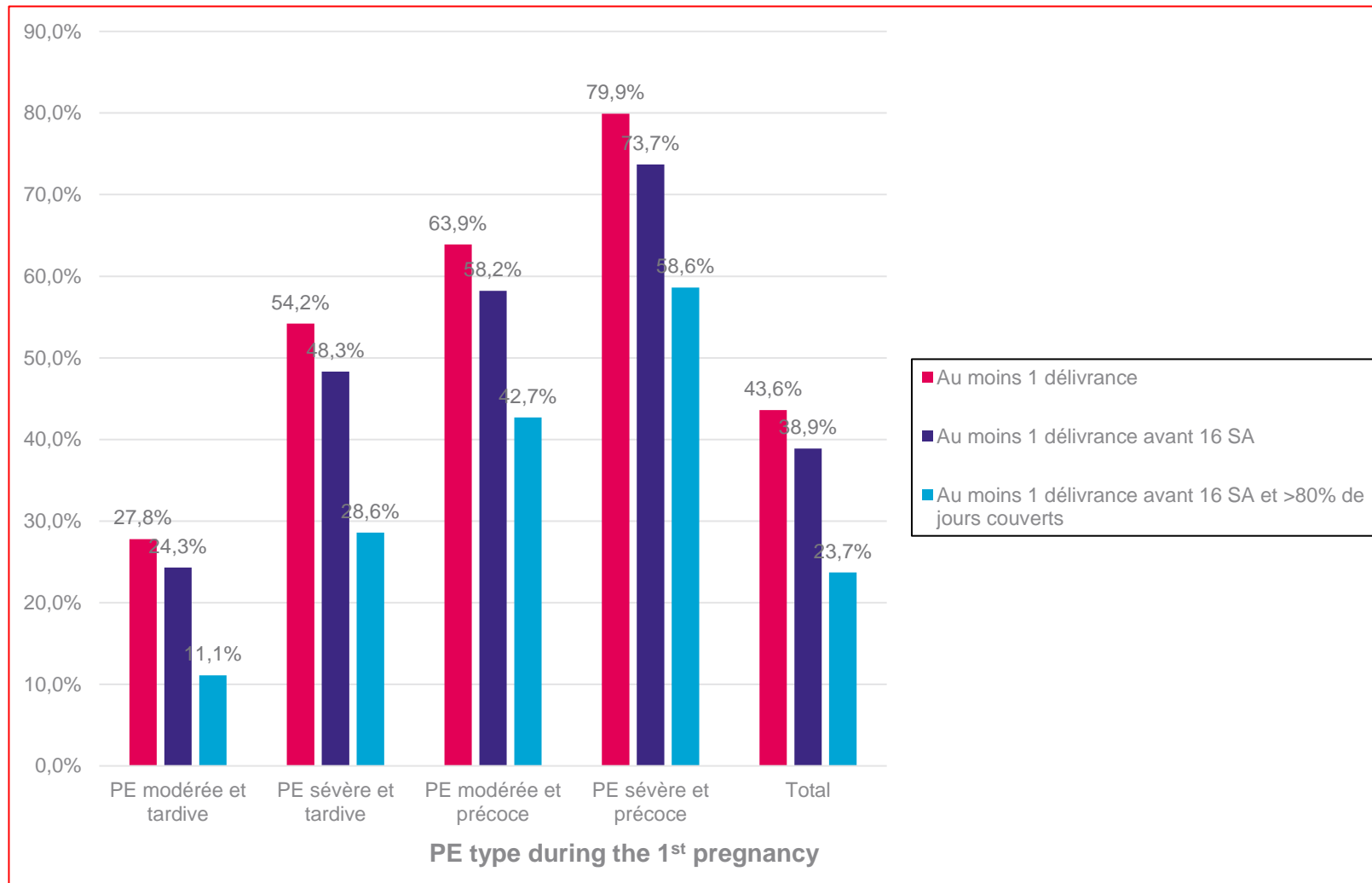
Drug class	Drug
ACE inhibitors	Benazepril
	Captopril
	Enalapril
	Quinapril
Calcium channel blockers	Diltiazem
	Nifedipine
	Verapamil
Beta-blockers	Labetalol
	Metoprolol
	Nadolol
	Oxprenolol
	Propranolol
	Timolol
Diuretics	Furosemide
	Hydrochlorothiazide
	Spirolactone
Other	Clonidine
	Hydralazine
	Methyldopa
	Minoxidil

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ACE, angiotensin-converting enzyme.



Lailier G, Grave C, Gabet A, Regnault N, Deneux-Tharaux C, Kretz S, Tsatsaris V, Plu-Bureau G, Blacher J, Olie V. Aspirin for the Prevention of Early and Severe Pre-Eclampsia Recurrence: A Real-World Population-Based Study. *Drugs*. 2023 Apr;83(5):429-437. doi: 10.1007/s40265-023-01842-3. Epub 2023 Mar 3. PMID: 36867398; PMCID: PMC10042896.



Lailier G, Grave C, Gabet A, Regnault N, Deneux-Tharaux C, Kretz S, Tsatsaris V, Plu-Bureau G, Blacher J, Olie V. Aspirin for the Prevention of Early and Severe Pre-Eclampsia Recurrence: A Real-World Population-Based Study. *Drugs*. 2023 Apr;83(5):429-437. doi: 10.1007/s40265-023-01842-3. Epub 2023 Mar 3. PMID: 36867398; PMCID: PMC10042896.

Adjusted IRR of having a PE during the 2nd pregnancy, according to aspirin use

	Mild & late PE (N=1 143)	Severe & early PE (N=463)	Total PE (N=2 447)
<u>Aspirin use</u>			
No aspirin	Ref	Ref	Ref
At least 1 use	1.06 (0.92 - 1.22)	0.77 (0.62 - 0.95)	0.98 (0.90-1.08)
At least 1 use ≤ 16 WG	1.04 (0.90 - 1.20)	0.71 (0.57 - 0.89)	0.93 (0.85-1.01)
At least 1 use ≤ 16 WG and ≥ 80% days covered	1.08 (0.92 - 1.27)	0.60 (0.47 - 0.77)	0.93 (0.86-1.01)
<u>Mean daily dose</u>			
No aspirin	Ref	Ref	Ref
0-75mg/d	1.02 (0.86 - 1.21)	1.10 (0.85 - 1.41)	1.03 (0.92-1.16)
75-100mg/d	1.05 (0.87 - 1.26)	0.77 (0.56 - 1.04)	0.99 (0.87-1.12)
≥ 100mg/d	1.03 (0.88 - 1.21)	0.67 (0.53 - 0.85)	0.95 (0.85-1.05)

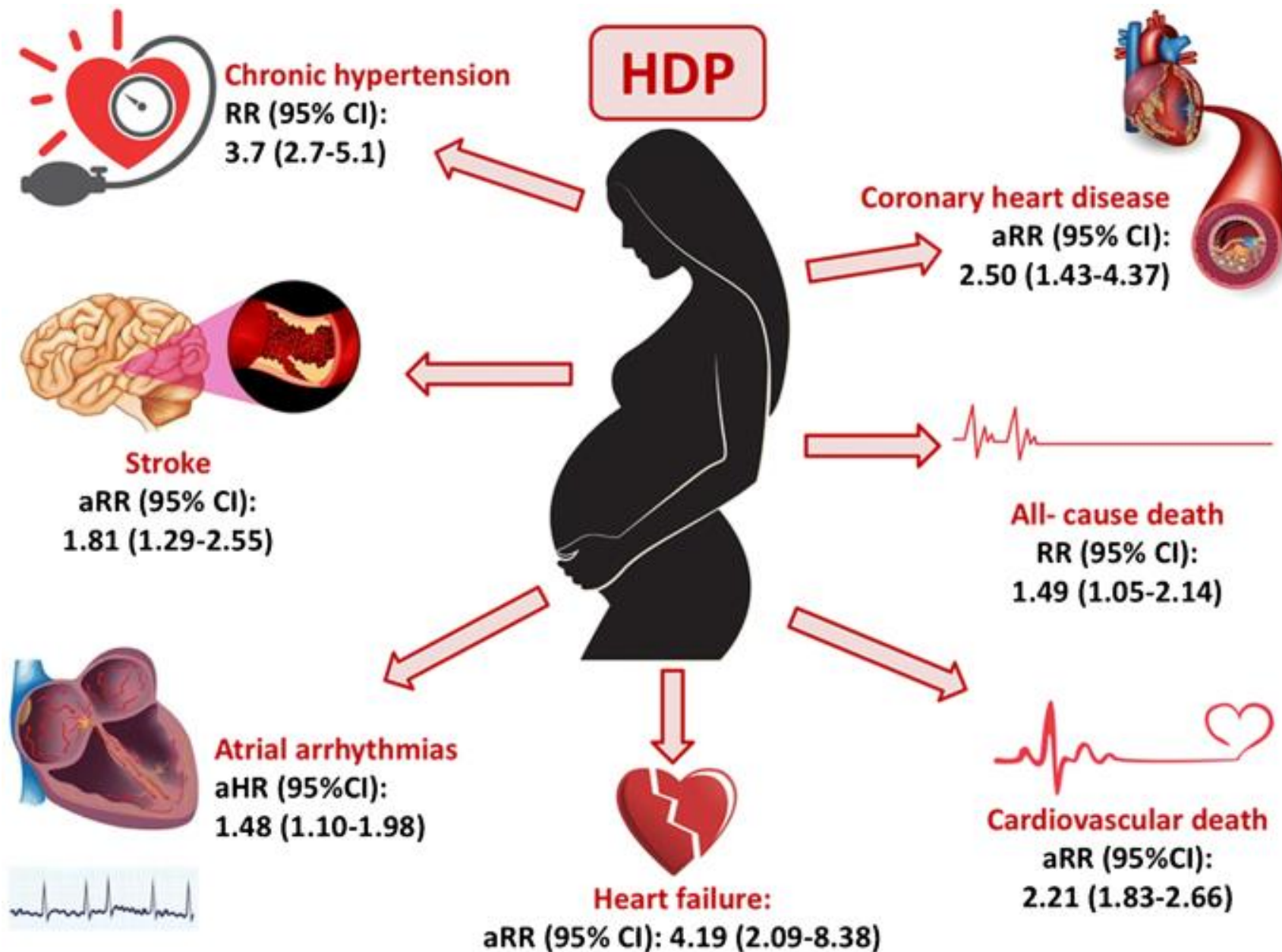



Fig. 1 : Estimated increase in the risk of chronic hypertension, cardiovascular diseases, and death after hypertensive disorders of pregnancy. After a hypertensive disorder of pregnancy, a woman is subject to a significantly increased risk of chronic hypertension, cardiovascular diseases, and death. These risk are independent of conventional cardiovascular risk factors. aHR adjusted hazard ratio, aRR adjusted risk ratio, HDP hypertensive disorders of pregnancy, RR relative risk.

Hypertensive disorders of pregnancy and onset of chronic hypertension in France: the nationwide CONCEPTION study

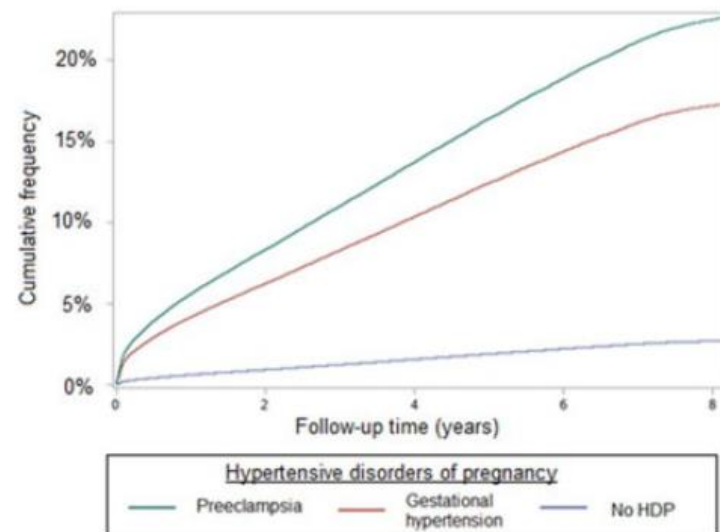
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Hypertensive disorders of pregnancy and onset of chronic hypertension
France 2010 - 2018



2,663,573 primiparous women

- 113,803 Gestational hypertension
- 66,260 Pre-eclampsia



Adjusted Hazard Ratios of developing chronic hypertension

- Gestational hypertension:
aHR = 6.03 (95%CI: 5.89-6.17)
- Pre-eclampsia:
aHR = 8.10 (95%CI: 7.88-8.33)

Hypertensive disorders of pregnancy increase the risk of developing chronic hypertension in primiparous women in the first years following delivery

En pratique

- DHG : situation fréquente
- Traiter toutes les HTA (>140/90 mmHg) chez les femmes enceintes
- Thérapeutiques de choix pendant la grossesse (et le post partum)
 - Labétalol
 - Nifedipine (nicardipine)
 - Alpha-méthylidopa
- Ne pas oublier l'aspirine
- Ces femmes doivent être surveillées toute leur vie !



MERCI à l'équipe CONCEPTION

- **Valérie Olié**
- **Grégory Lailler**
- **Amélie Gabet**
- **Clémence Grave**
- **Nolwenn Regnault**
- **Alice Martin**
- **Elodie Moutengou**
- **Laure Carcaillon-Bentata**
- **Pierre Joly**

- **Yannick Bejot**
- **Catherine Deneux-Tharaux**
- **Sandrine Kretz**
- **Vassilis Tsatsaris**
- **Geneviève Plu-Bureau**
- **Jacques Blacher**