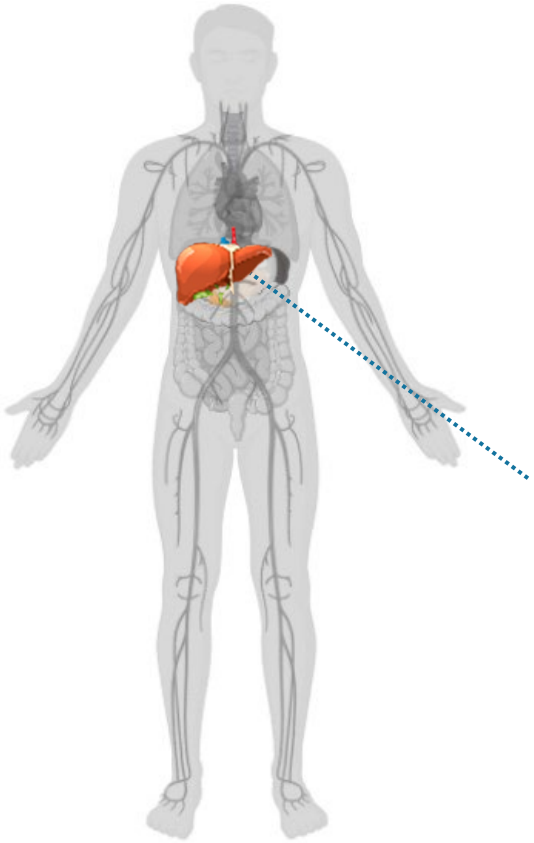
Metabolic Dysregulation in Hypercortisolism

Hypercortisolism is associated with several metabolic impairments

Physiologic role of cortisol[1]



Liver and Adipose Metabolism

- **Glucose and lipid metabolism**

Consequences of excess cortisol

Up to 64%
Abnormal glucose tolerance[2]

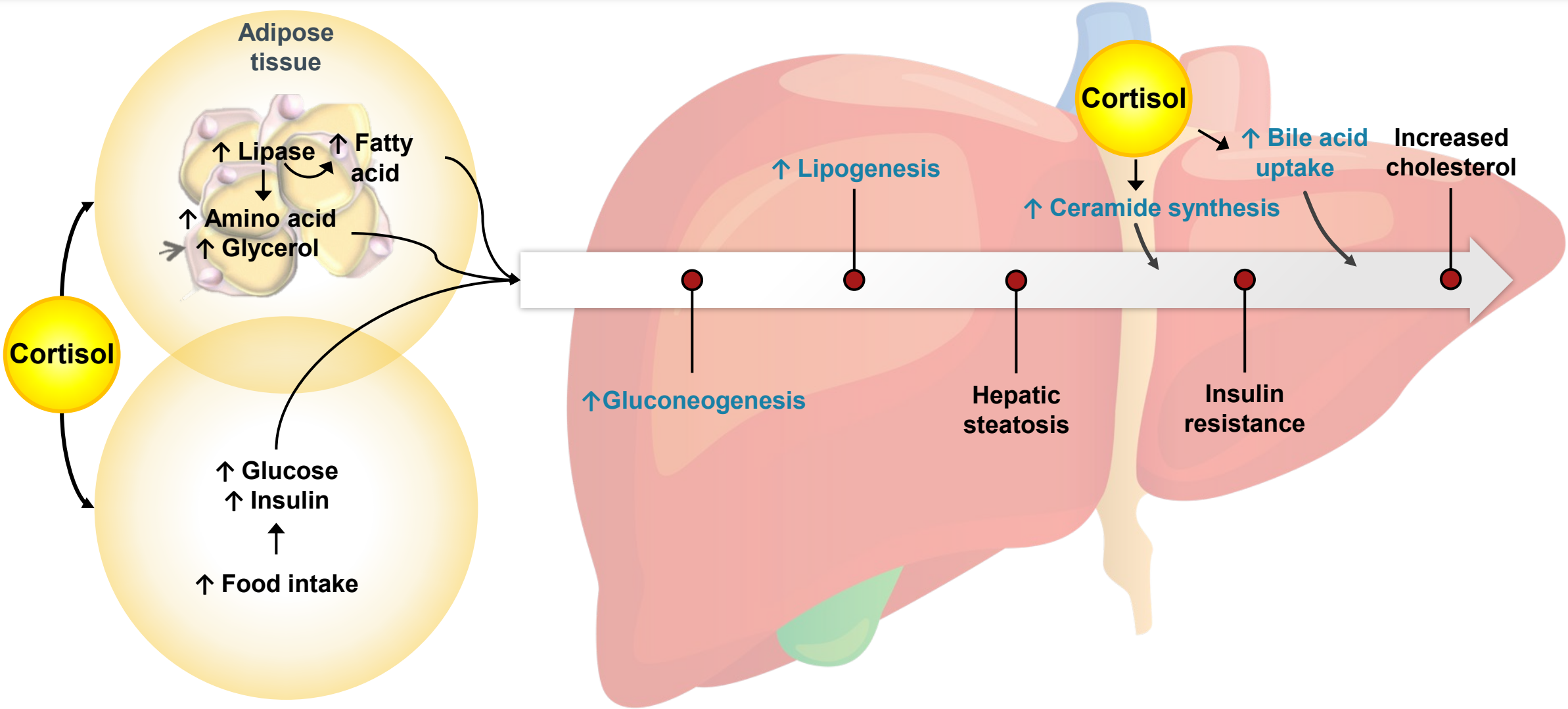
Up to 47%
Diabetes[2]

Up to 71%
Dyslipidemia[2]

Up to 100%
Visceral obesity[3]

1. Cruz-Topete D, et al. *Front Endocrinol*. 2020;11:347. doi:10.3389/fendo.2020.00347 2. Braun LT, et al. *Front Endocrinol (Lausanne)*. 2019;10:766.
3. Pivonello R, et al. *Lancet Diabetes Endocrinol*. 2016;4:611-629.

Excess cortisol stimulates lipogenesis and dysregulates cholesterol metabolism[1-3]

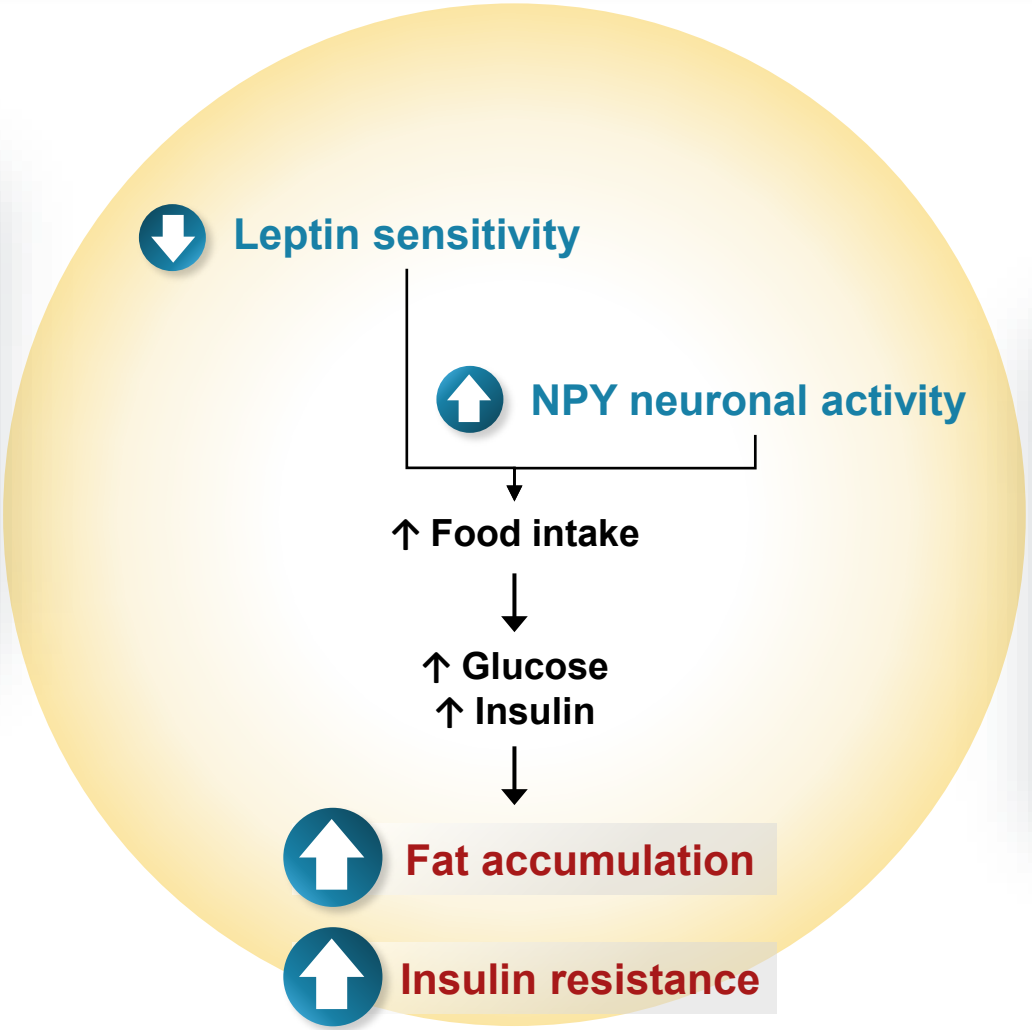


1. Rahimi L, et al. *Diabetes Metab Syndr Obes*. 2020;13:1133-1145. 2. Ormazabal V, et al. *Cardiovasc Diabetol*. 2018;17:122. 3. Magomedova L, Cummins CL. *Handb Exp Pharmacol*. 2016;233:73-93.

Excess cortisol can increase food intake and fat accumulation[1,2]

Leptin

- Leptin **reduces appetite** under normal conditions
- Excess cortisol **reduces sensitivity to leptin**, leading to hyperphagia



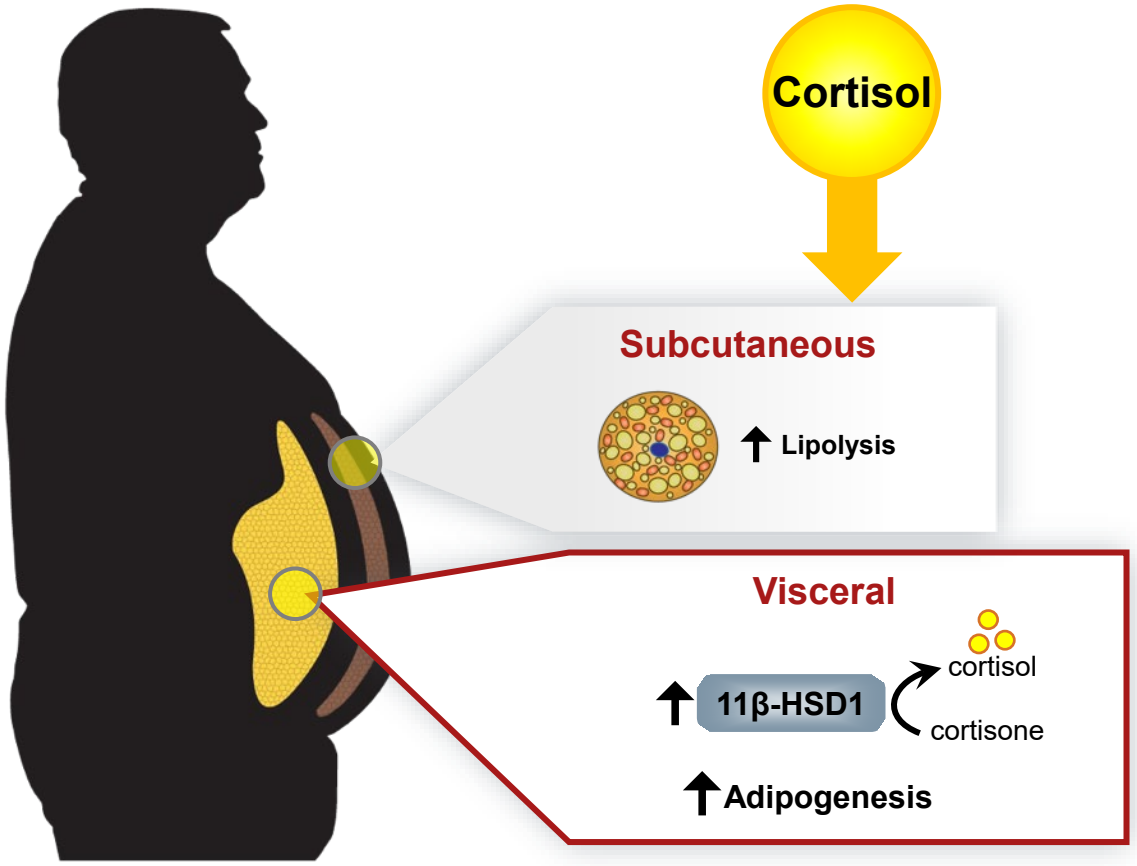
Neuropeptide Y (NPY)

- NPY **stimulates appetite** under normal conditions
- Excess cortisol **increases NPY neuronal activity**, leading to increased food consumption

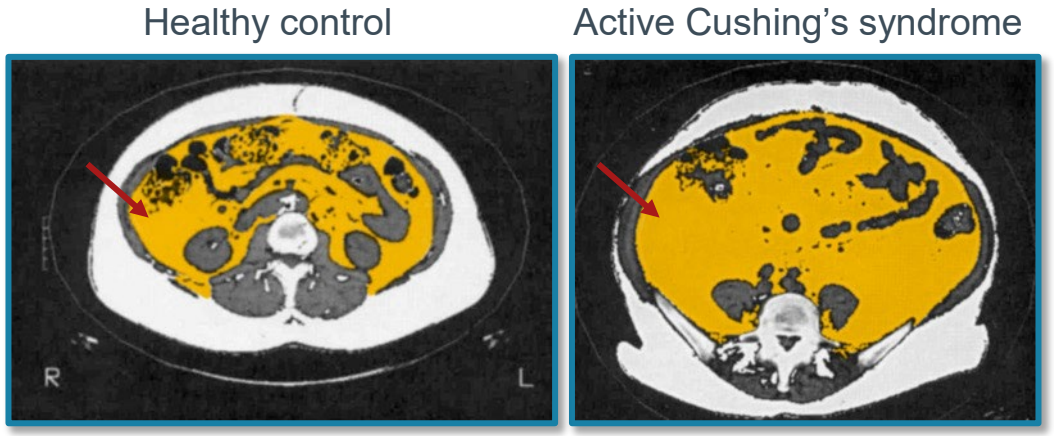
1. Rahimi L, et al. *Diabetes Metab Syndr Obes*. 2020;13:1133-1145. 2. Geer EB, et al. *Endocrinol Metab Clin North Am*. 2014;43:75-102.

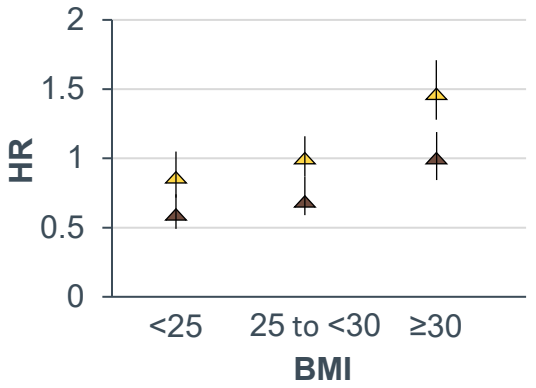
Excess cortisol can cause visceral fat accumulation without obvious obesity

Effects of Cortisol on Adipose Tissues[1,2]



Abdominal CT scan showing increased adipose deposition[2]





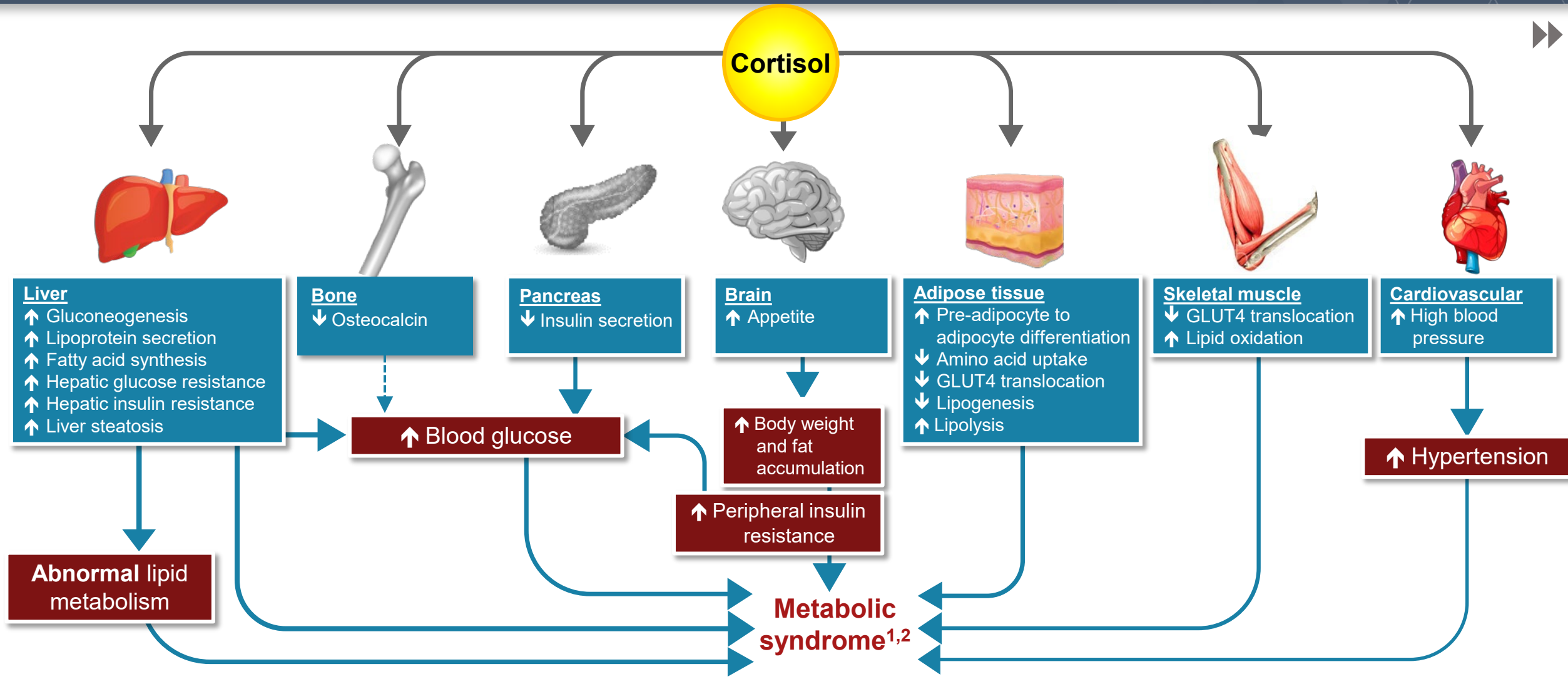
Mortality (HR ± 95% CI)[a] in women with visceral vs subcutaneous abdominal fat[3]

△ Visceral fat
▲ Subcutaneous fat

BMI=body mass index; CT=computed tomography; HR=hazard ratio; HSD=hydroxysteroid dehydrogenase.
[a]Adjusted for age, education, smoking status, physical activity, alcohol consumption, type 2 diabetes, and coronary heart disease.

1. Magomedova L, Cummins CL. *Handb Exp Pharmacol.* 2016;233:73-93. 2. Peeke PM, Chrousos GP. *Ann N Y Acad Sci.* 1995;771:665-676. 3. Koster A, et al. *Obesity (Silver Spring).* 2015;23(4):893-897.

Excess cortisol contributes to the development of metabolic syndrome



GLUT4=glucose transporter type 4.

1. Pivonello R, et al. *Lancet Diabetes Endocrinol*. 2016;4:611-629. 2. Barbot M, et al. *Front Endocrinol (Lausanne)*. 2018;9:284.