



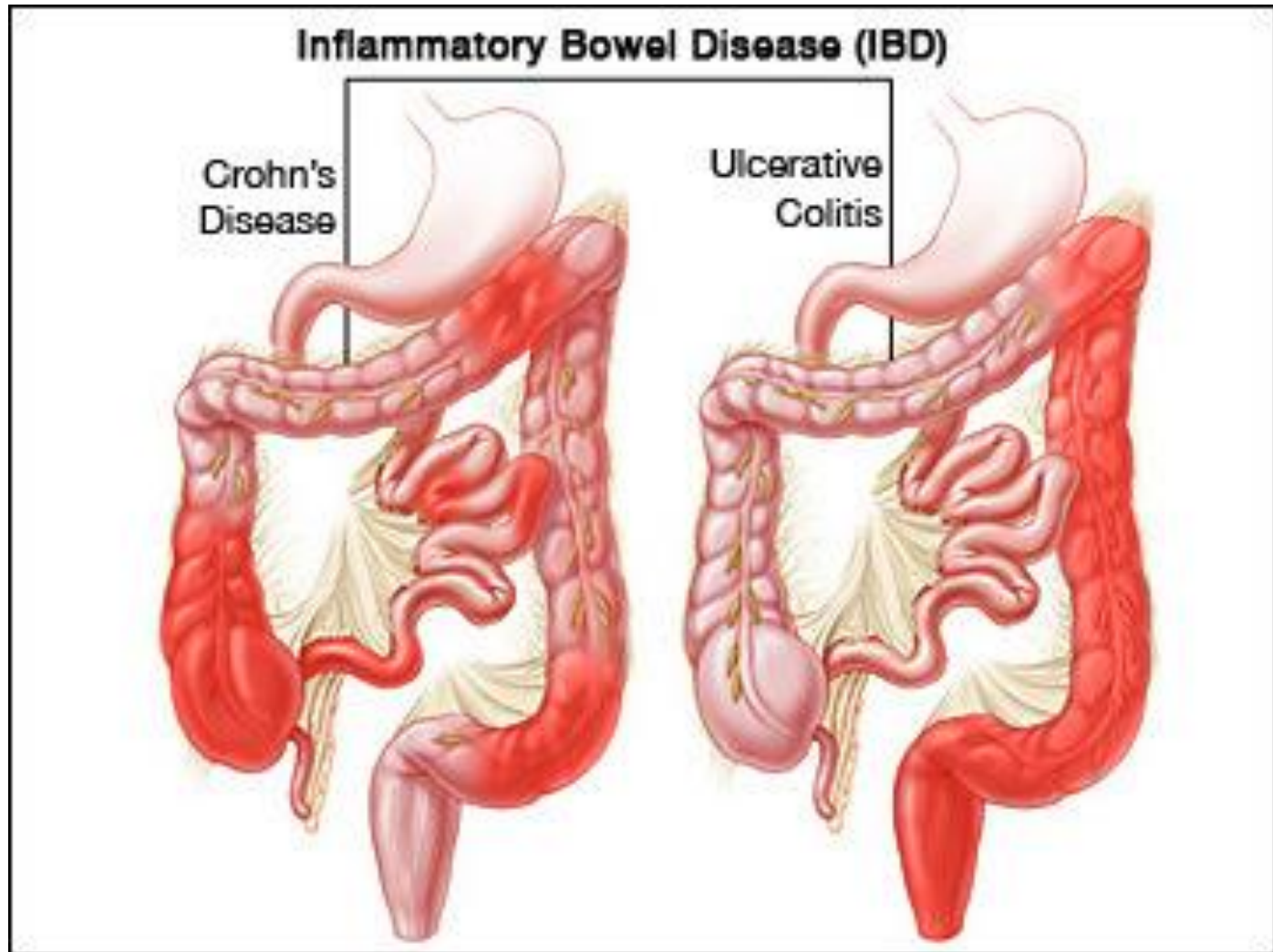
SMCCV
Schweizerische Morbus Crohn / Colitis ulcerosa Vereinigung

ASMCC
Association Suisse de la Maladie de Crohn et Colite ulcéreuse

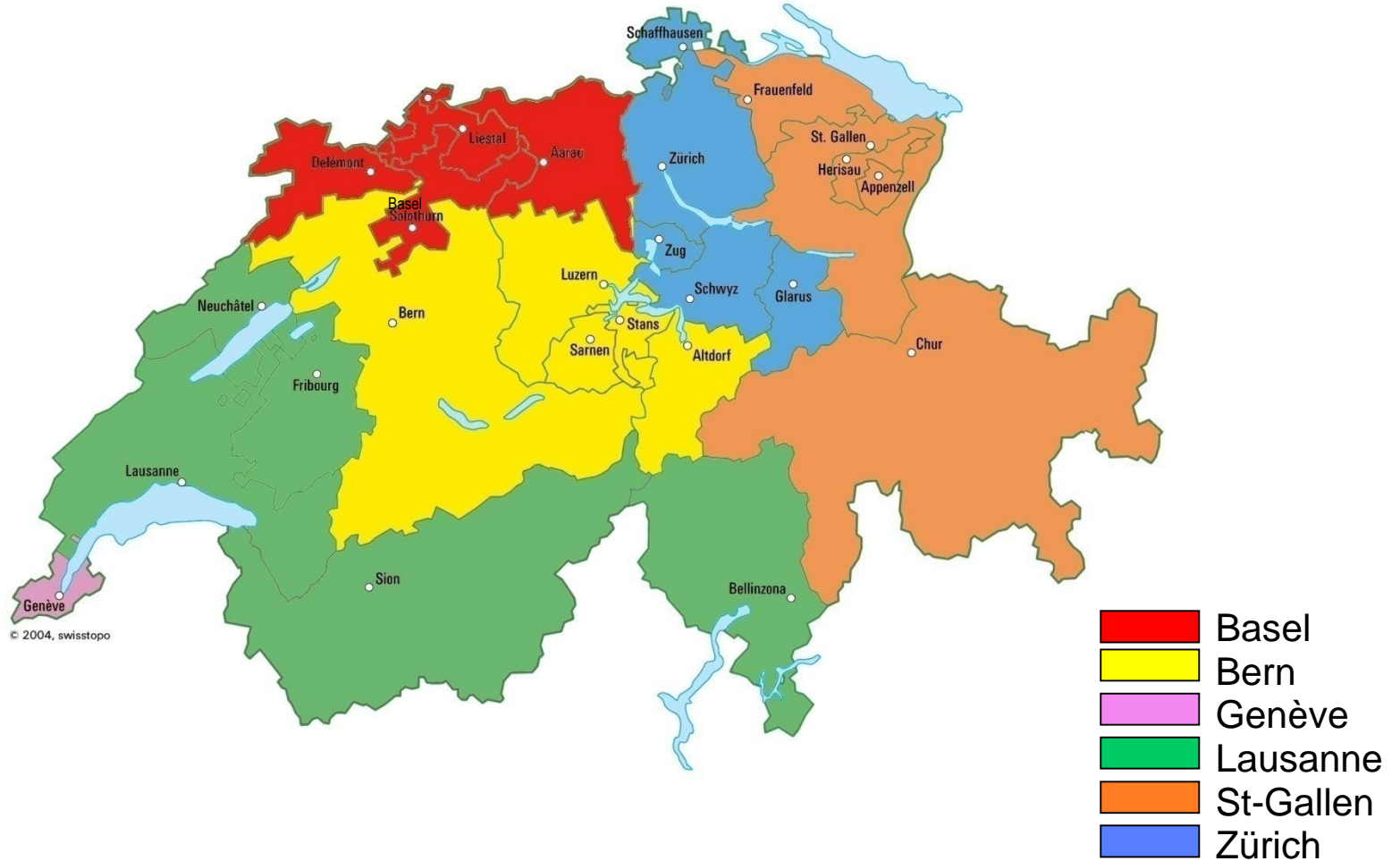
Impact de l'environnement pour les MICI

Prof. Dr. Alain Schoepfer,
Médecin Chef, GLG, CHUV

MICI: maladies inflammatoires chroniques intestinales



SWISS IBD cohort study



SWISS IBD cohort study

Fréquence:






M. de Crohn: 1/1000

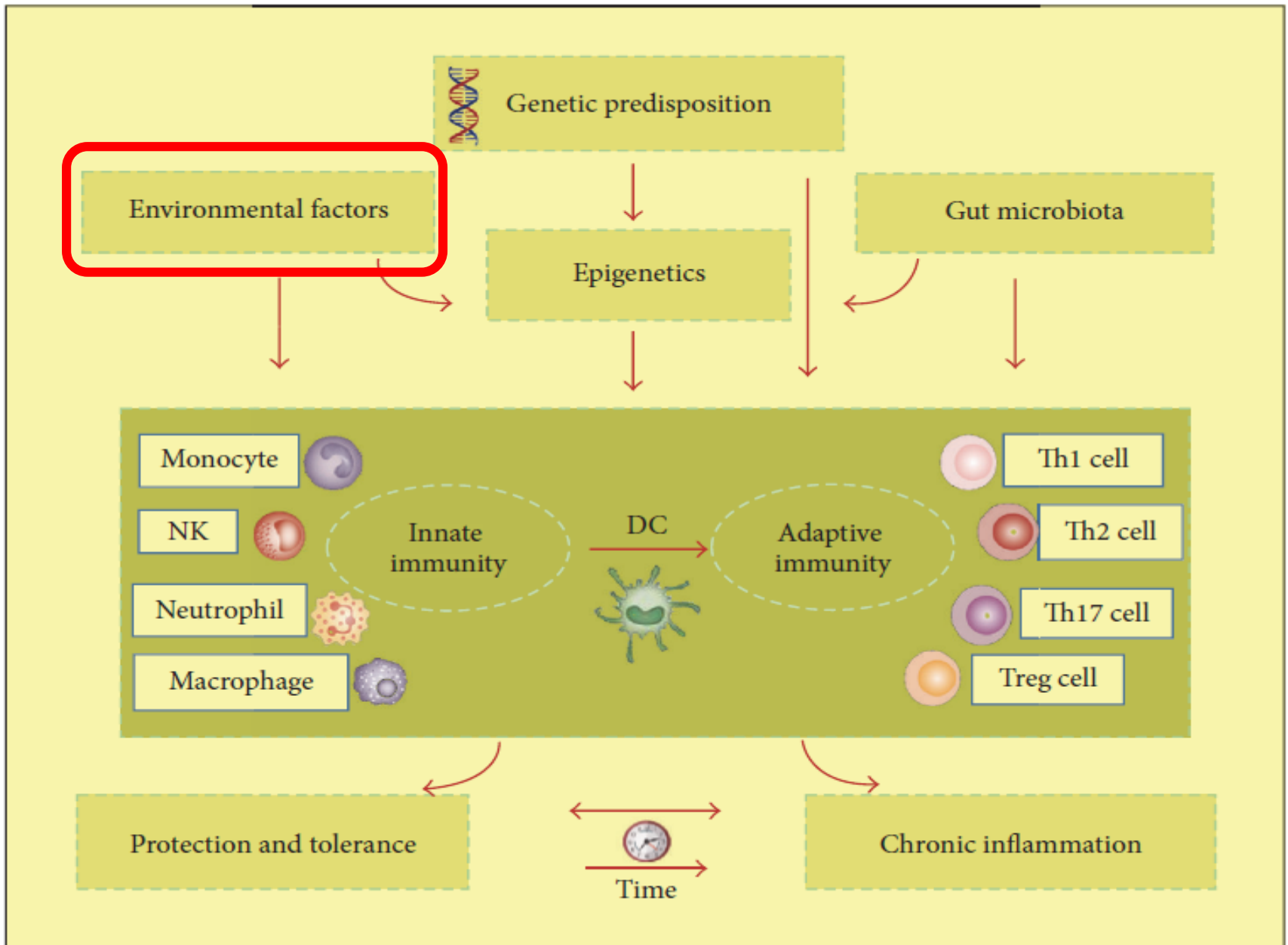
Colite ulcéreuse: 1/1000

MICI: 1/500

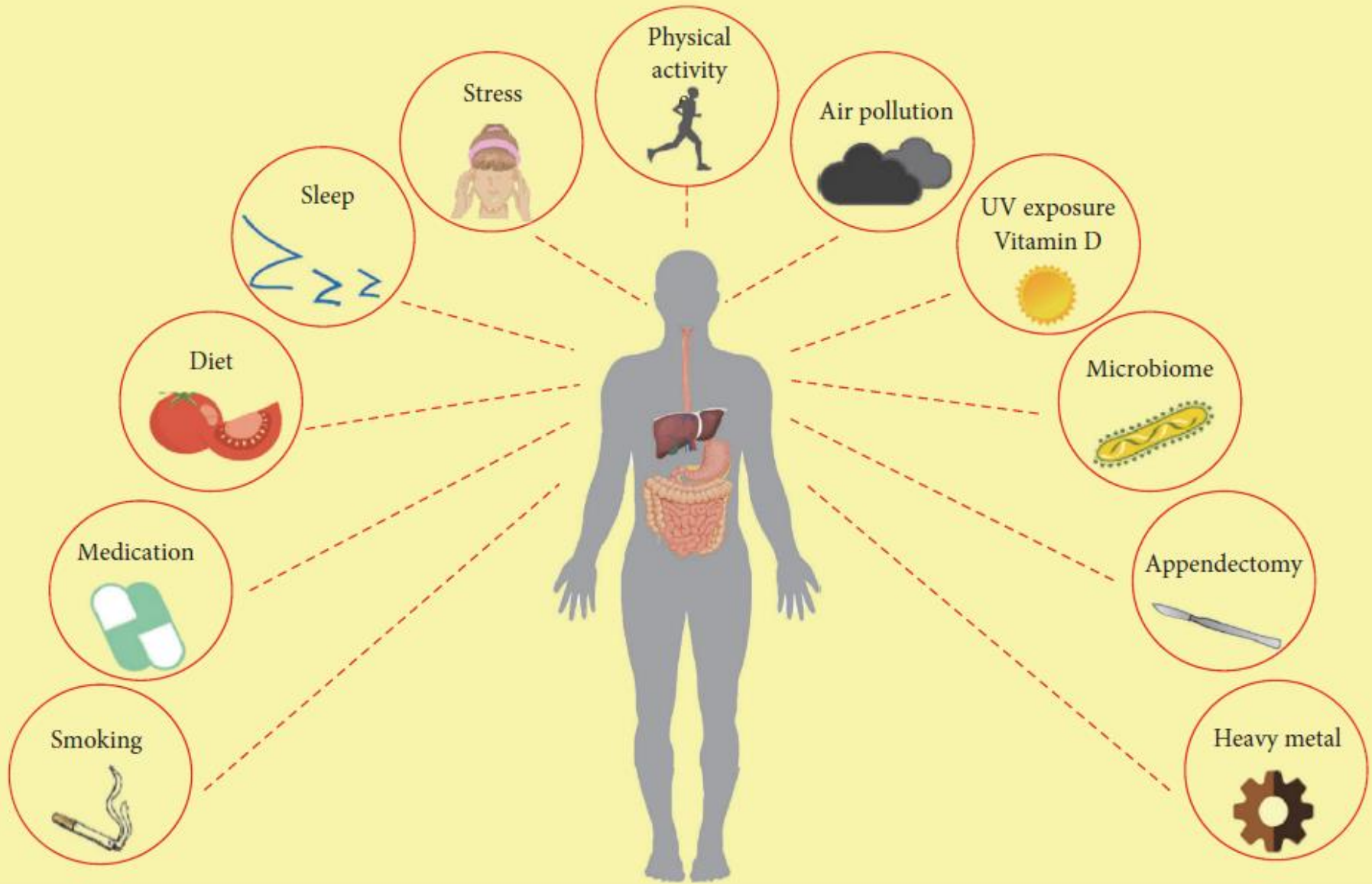
Au niveau Suisse: 16'000 patients



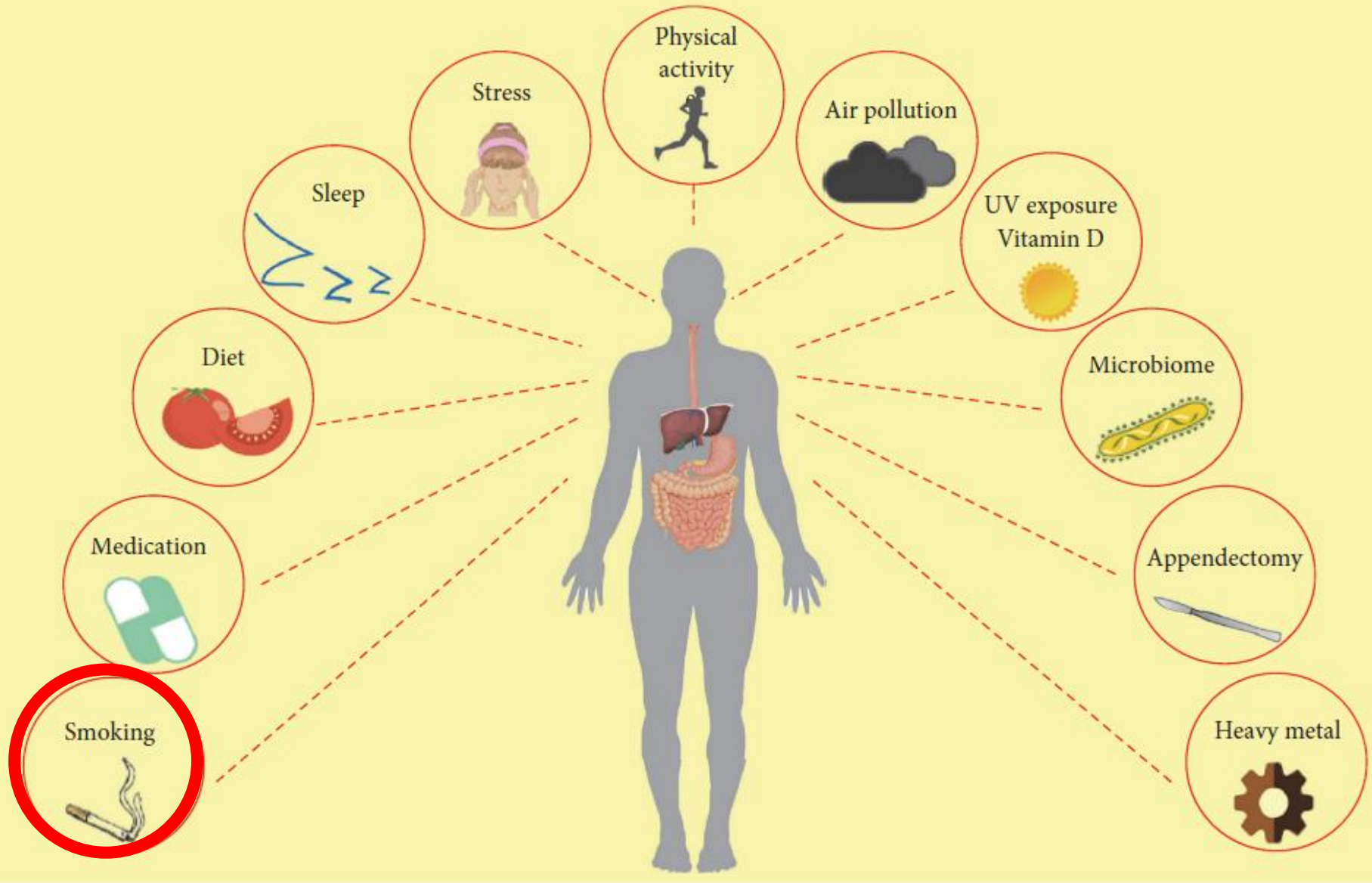
	Bern
	Genève
	Lausanne
	St-Gallen
	Zürich



Environmental risk factors



Environmental risk factors





Maladie de Crohn



Colite ulcéreuse

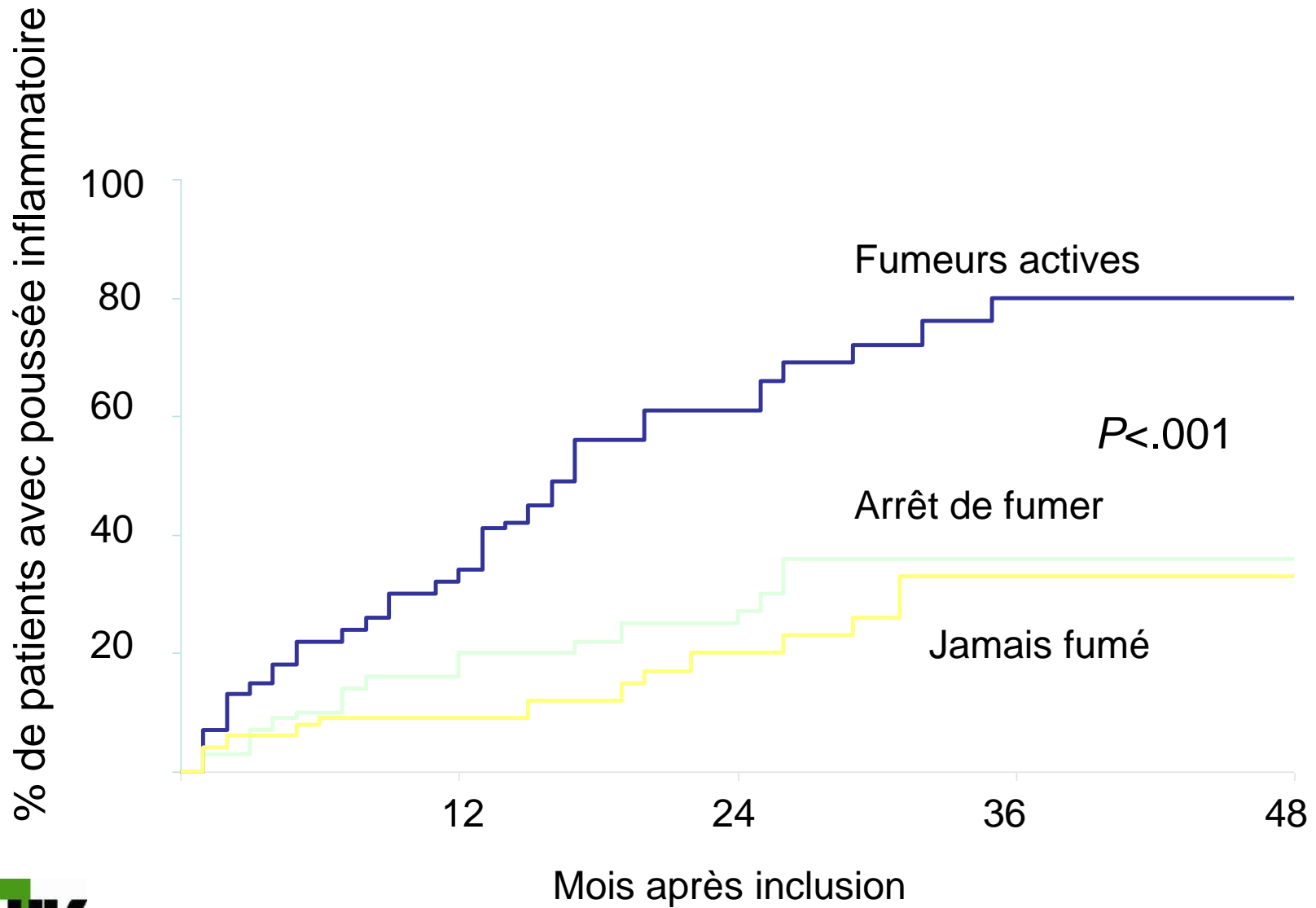


	RCUH		M. Crohn	
	<i>cigarettes*</i>	<i>arrêt‡</i>	<i>cigarettes*</i>	<i>arrêt‡</i>
Développement	↓	↑	↑	±
Poussées	↓	↑	↑	↓
Chirurgie	↓	-	↑	↓

* Current smoking compared to non-smoking.

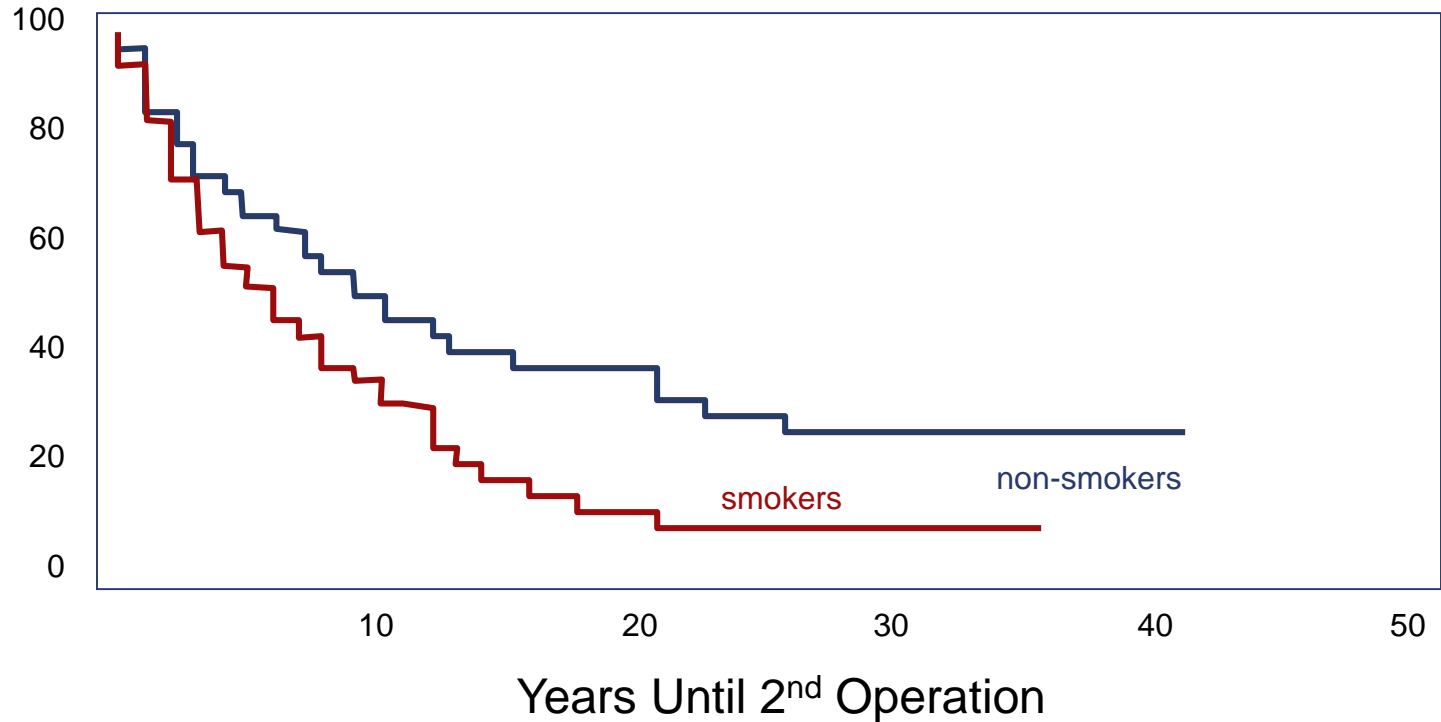
‡ Smoking cessation compared to continuing smoking.

Effet des cigarettes sur l'évolution de la M. Crohn



Fumer et risque pour 2ème opération dans la M. Crohn

Survival Functions



	<u>Log Rank</u>	<u>Degrees of Freedom</u>	<u>P</u>
Smokers vs Non-smokers	5.76	1	.0164

Cigarette «classique»



Cigarette électrique



Mécanisme
d'action

- Combustion
- goudron,
- beaucoup de substances cancérogènes

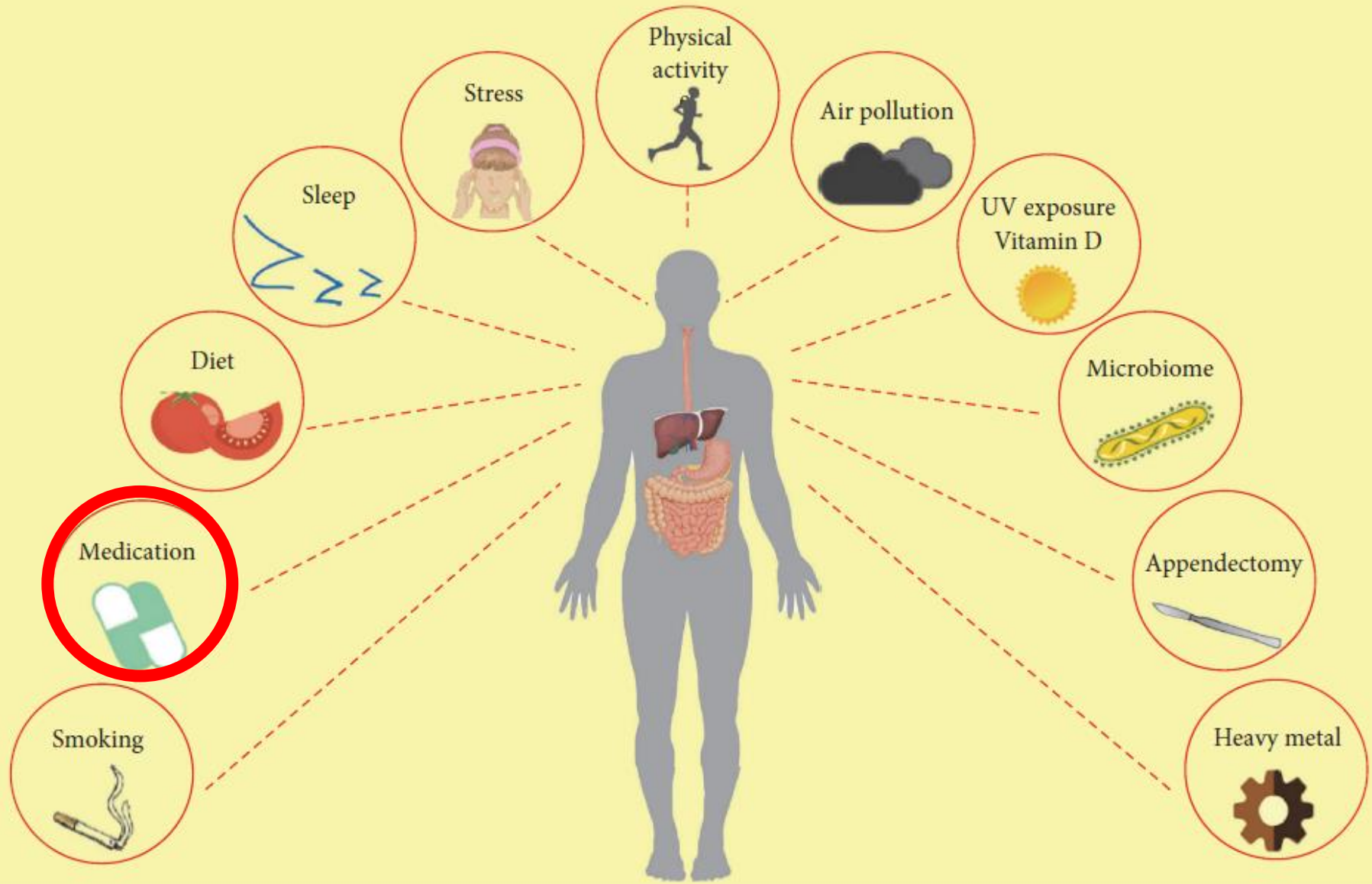
- Pas de combustion
- Vaporisation
- Liquide: propylenglycole, glycérine, arômes, eau, +/- nicotine

Effet sur les
MICI

- Beaucoup de données

??

Environmental risk factors



Médicaments, pilule (anticonceptive)



Médicaments, pilule (anticonceptive)

	Crohn's Disease (CD)	UC	Controls (Ct)	Odds Ratio (95%CI); <i>p</i> Value
Ever smoking	54.7%	54.4%	45.7%	1.78 (1.32–2.41); <i>p</i> = 0.0002 CD vs Ct 1.66 (1.17–2.35); <i>p</i> = 0.004 UC vs Ct
Smoking now	29.0%	15.7%	19.0%	1.96 (1.38–2.78); <i>p</i> = 0.0001 CD vs Ct 2.27 (1.47–3.50); <i>p</i> = 0.0002 CD vs UC
User of ASA regularly* ever (Y/N)	12.0%	14.3%	13.4%	0.91 (0.58, 1.43); <i>p</i> = 0.69 CD vs Ct 0.89 (0.54, 1.46); <i>p</i> = 0.76 UC vs Ct
User of acetaminophen regularly* ever (Y/N)	47.5%	33.3%	31.4%	2.27 (1.67, 3.11); <i>p</i> < 0.0001 CD vs Ct 1.18 (0.82, 1.70); <i>p</i> = 0.38 UC vs Ct
User of any other pain killer regularly* ever (Y/N)	29.7%	18.7%	18.5%	2.18 (1.53, 3.11); <i>p</i> < 0.0001 CD vs Ct 1.08 (0.70, 1.68); <i>p</i> = 0.71 UC vs Ct
User ever of OCP**	88%	90%	86%	0.98 (0.56, 1.72); <i>p</i> = 0.95 CD vs Ct 1.06 (0.53, 2.13); <i>p</i> = 0.86 UC vs Ct
Number of years of OCP use between:				
15–19	2.8 (1.4)	2.5 (1.3)	2.3 (1.6)	1.21 (1.04, 1.42) <i>p</i> =0.02 CD vs Ct
20–24	3.7 (1.4)	3.2 (1.2)	3.3 (1.2)	1.28 (1.08, 1.51); <i>p</i> = 0.004 CD vs Ct
25–29	3.5 (1.4)	3.0 (1.4)	3.0 (1.3)	1.33 (1.10, 1.61); <i>p</i> = 0.004 CD vs Ct
30–34	3.2 (1.6)	2.4 (1.3)	2.5 (1.4)	1.44 (1.11, 1.88); <i>p</i> = 0.006 CD vs Ct
35–39	2.8 (1.6)	2.0 (1.2)	2.3 (1.4)	1.26 (0.84, 1.88); <i>p</i> = 0.26 CD vs Ct
15–39	8.0 (4.9)	6.7 (3.9)	6.6 (4.6)	1.07 (1.03, 1.11); <i>p</i> = 0.0009 CD vs Ct 1.06 (0.89, 1.26); <i>p</i> = 0.52 UC vs Ct

*Regular use of ASA and acetaminophen referred to at least twice per week.

** OCP refers to oral contraceptive pill. Questions about OCP were only asked of females.

Médicaments, pilule (anticonceptive)

Crohn's
Disease (CD)

UC

Controls
(Ct)

Odds Ratio (95%CI);
p Value

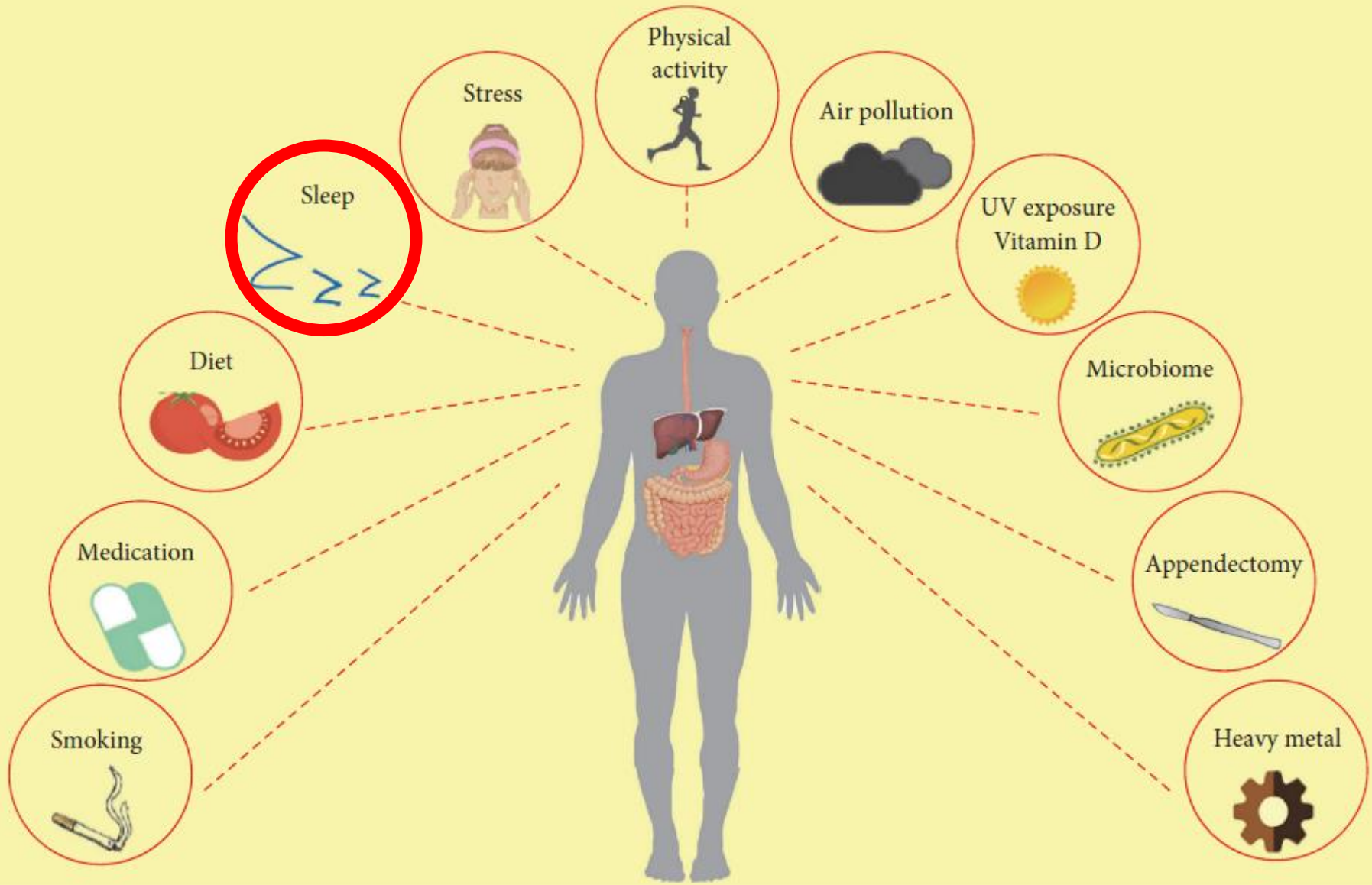
Médicaments anti-inflammatoires (par ex. Voltaren) sont un facteur de risque pour M. Crohn et RCUH

La pilule est un facteur de risque pour la M. Crohn

*Regular use of ASA and acetaminophen referred to at least twice per week.

** OCP refers to oral contraceptive pill. Questions about OCP were only asked of females.

Environmental risk factors

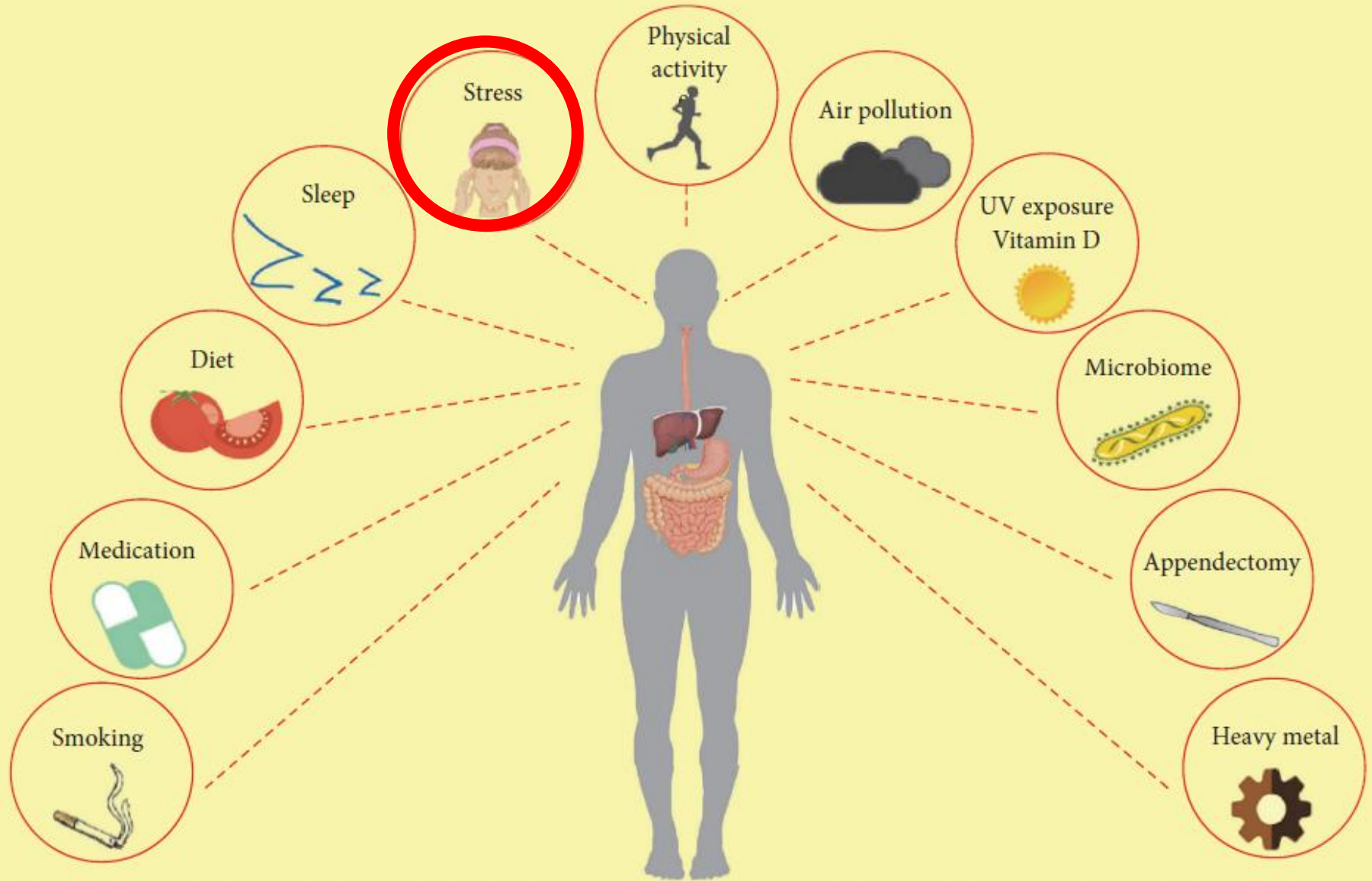


Sommeil et MICI



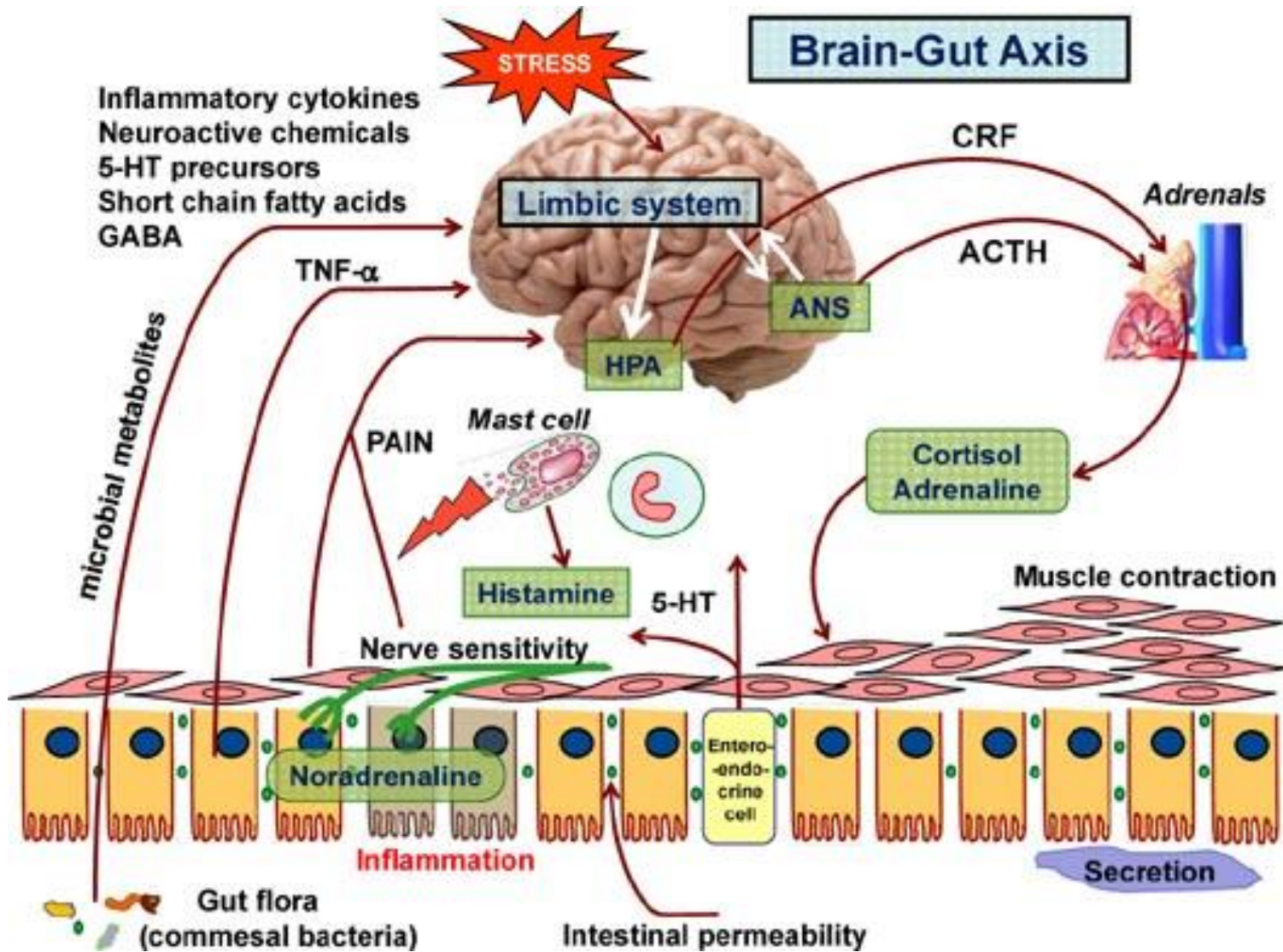
- Plus fréquemment des troubles du sommeil
- Manque de sommeil peut déclencher des poussées inflammatoires
- Implications pratiques:
 - discuter du problème
 - chercher les conditions qui peuvent y contribuer (syndrome d'apnée du sommeil, restless legs syndrome, etc).

Environmental risk factors

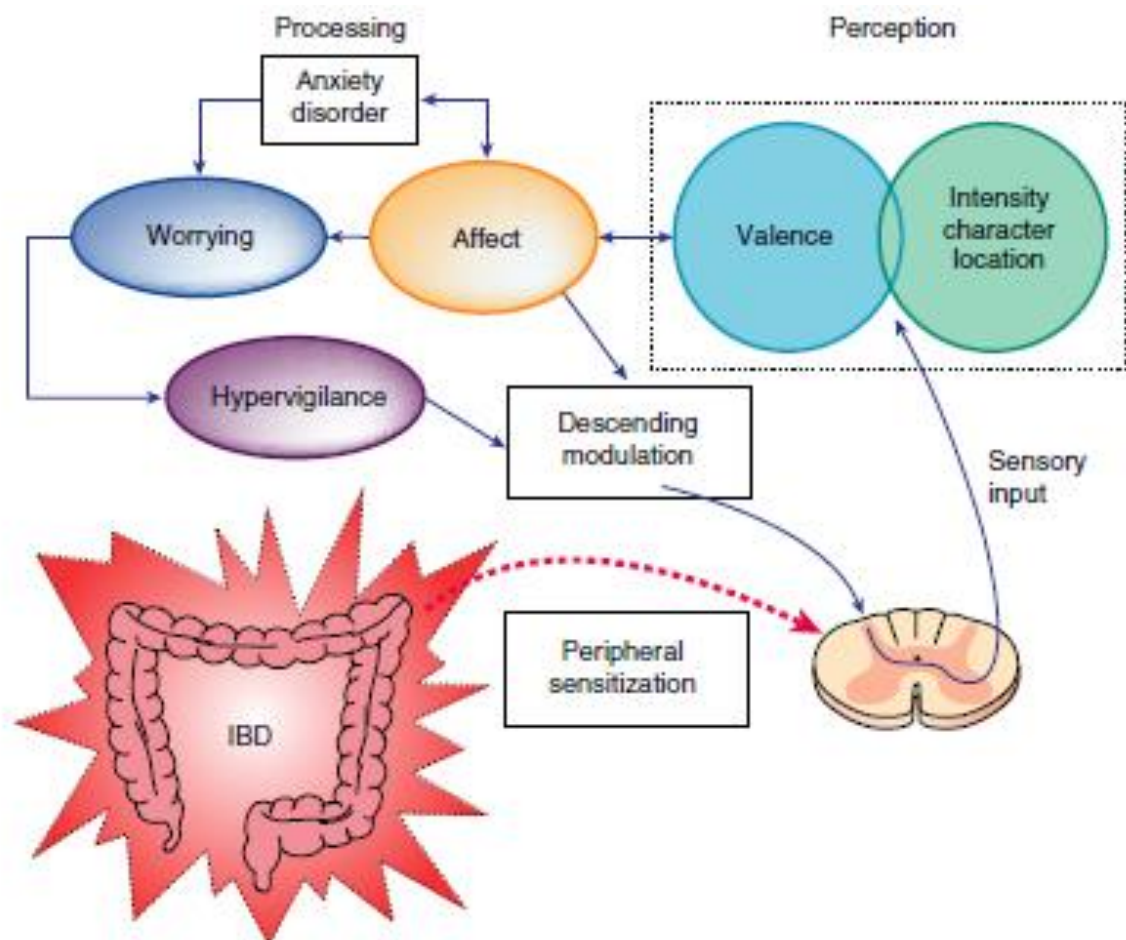


Stress et MICI: relation compliquée

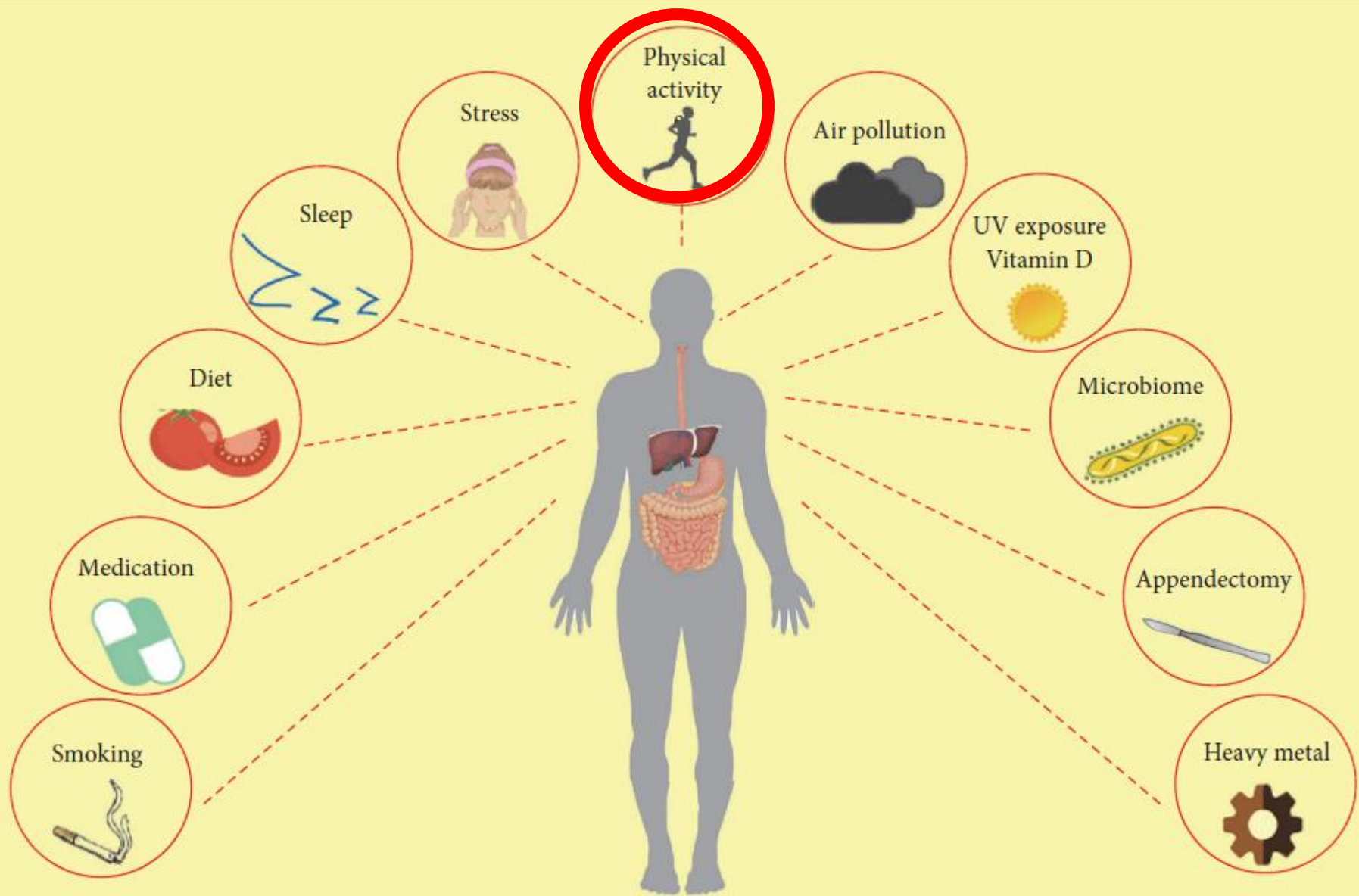




Stress peut intensifier la douleur



Environmental risk factors



Activité physique



Activité physique: études interventionnelles avec patients MC

- Intervention pendant 3 mois (low-intensity walking program)^{1,2}
 - Perte pondérale
 - État psychologique amélioré
 - Qualité de vie améliorée
 - Pas d'effet défavorable sur la M. Crohn
- Intervention pendant 12 mois (home-based low-impact exercise)³
 - Masse osseuse légèrement augmentée (trend)
 - Pas d'effet défavorable sur la M. Crohn

1. Loudon CP et al. *Am J Gastroenterol.* 1999;94:697-703.

2. Ng V et al. *Clin J Sport Med.* 2007;17:384-388.

3. Robinson RJ et al. *Gastroenterology.* 1998;115:36-41.

Activité physique: études interventionnelles avec patients MC

- Intervention pendant 3 mois (low-intensity walking program)^{1,2}

Activité physique légère, mais régulière, peut améliorer la qualité de vie et l'état psychologique

Intervention pendant 12 mois (même basée low impact exercise³

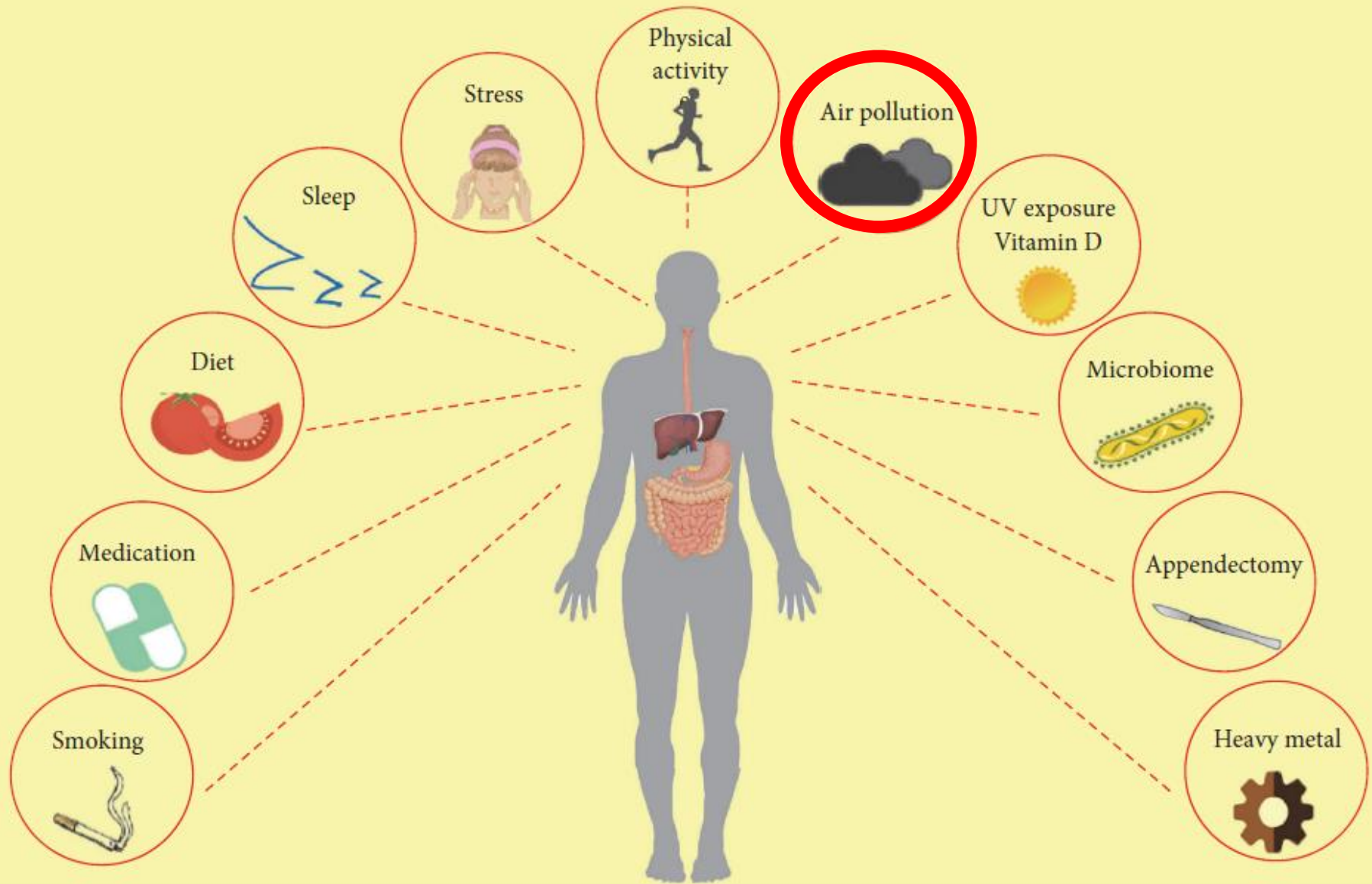
- Masse osseuse légèrement augmentée (trend)
- Pas d'effet défavorable sur la M. Crohn

1. Loudon CP et al. *Am J Gastroenterol.* 1999;94:697-703.

2. Ng V et al. *Clin J Sport Med.* 2007;17:384-388.

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Environmental risk factors





Association des MICI avec...

- Milieu urbain
- Pollution aérienne (NO₂, SO₂, CO)

Ananthkrishnan AN, et al. Nature Rev Gastroenterol Hepatol 2018;15:39-39

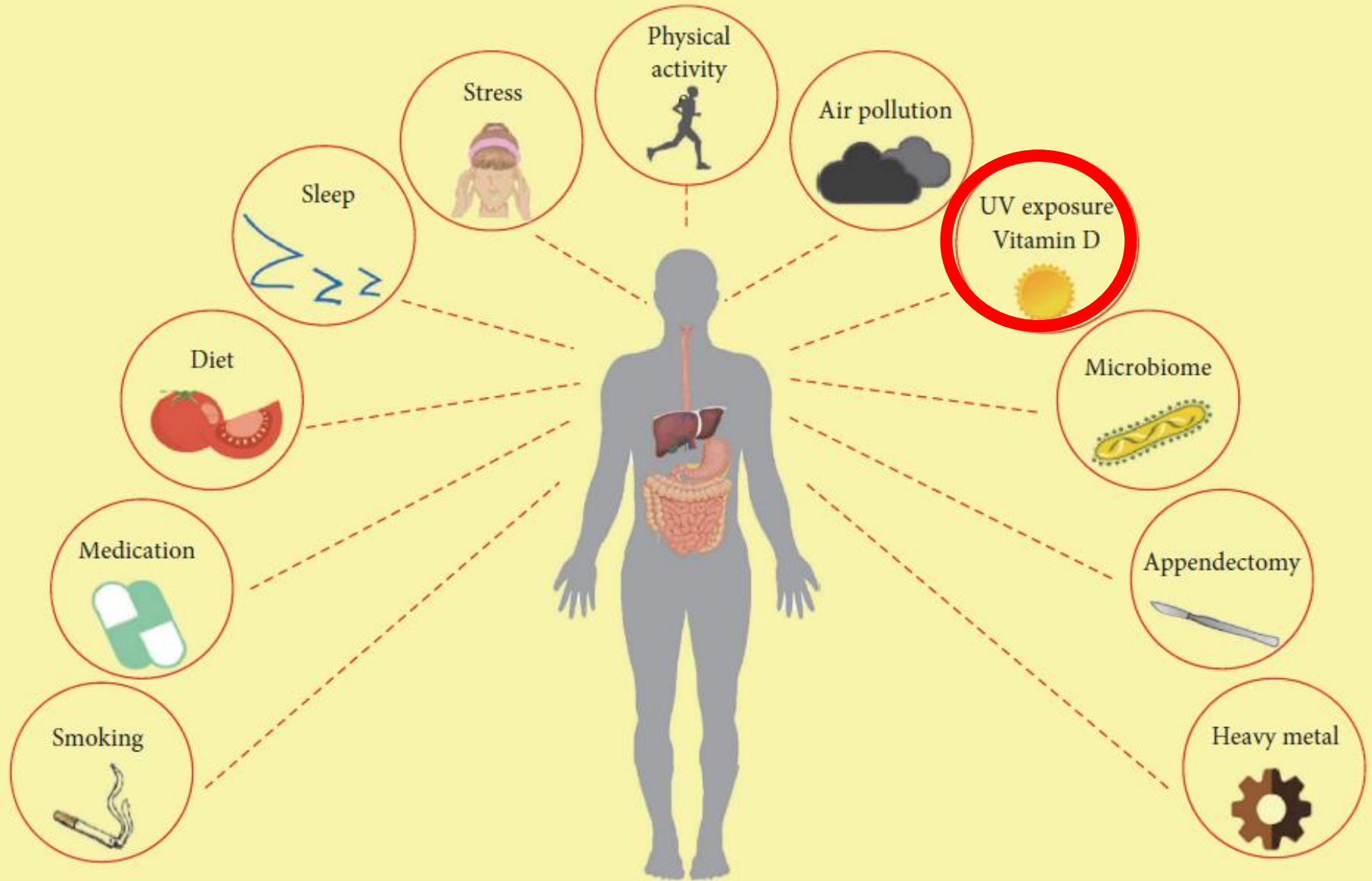
Association des MICI avec...

- Milieu urbain
- Pollution aérienne (NO₂, SO₂, CO)

Ananthkrishnan AN, et al. Nature Rev Gastroenterol Hepatol 2018;15:39-39



Environmental risk factors



Vitamine D

SUNLIGHT
The body itself makes
vitamin D when it is
exposed to the sun

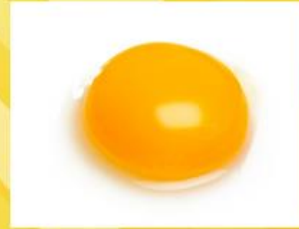
10 Best Vitamin D Rich Foods



Fortified Cereals



Orange Juice



Egg Yolk



Mushroom



Ricotta Cheese



Fatty Fish



COD Liver Oil

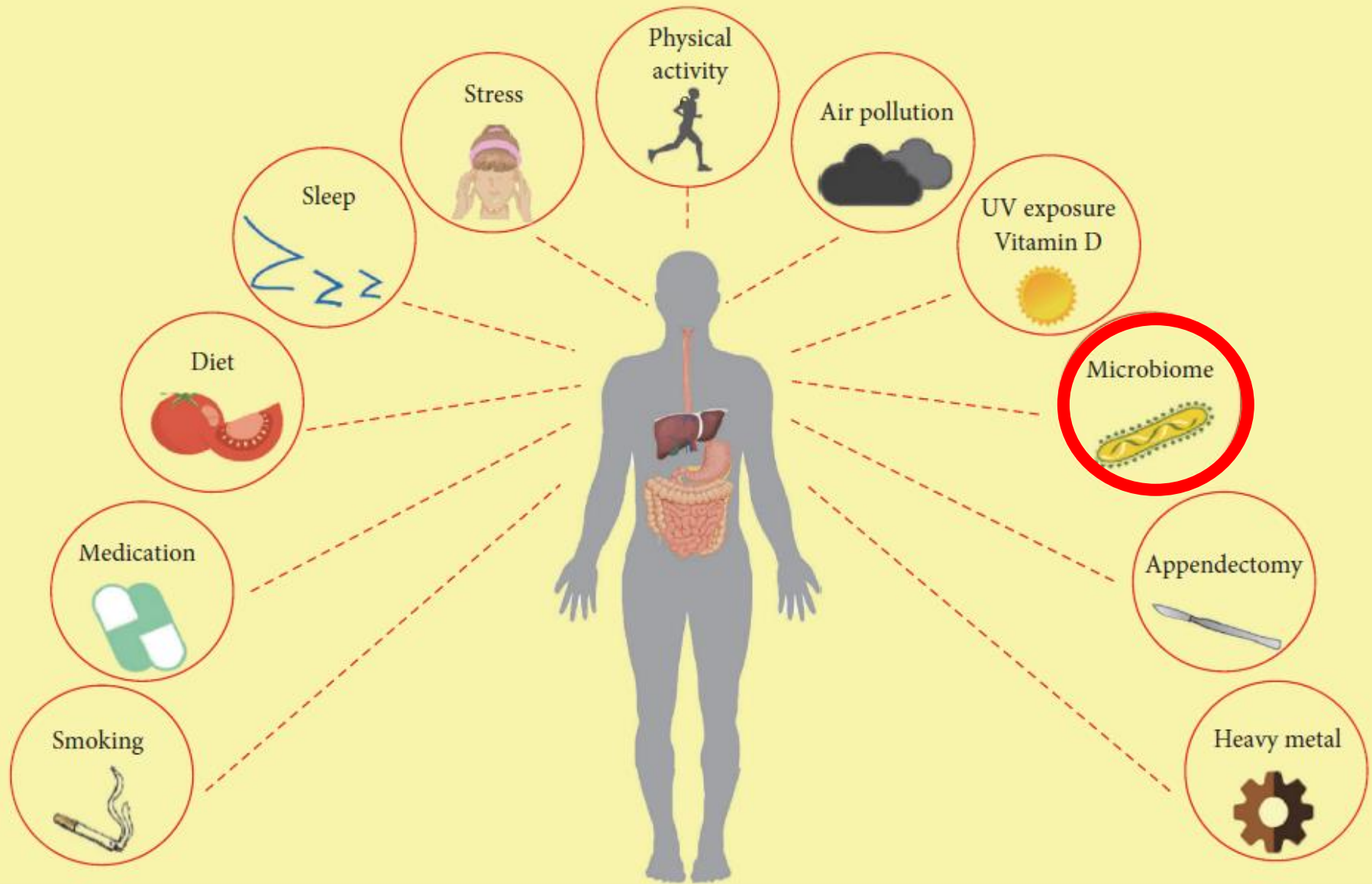


Cavier (Fish eggs)

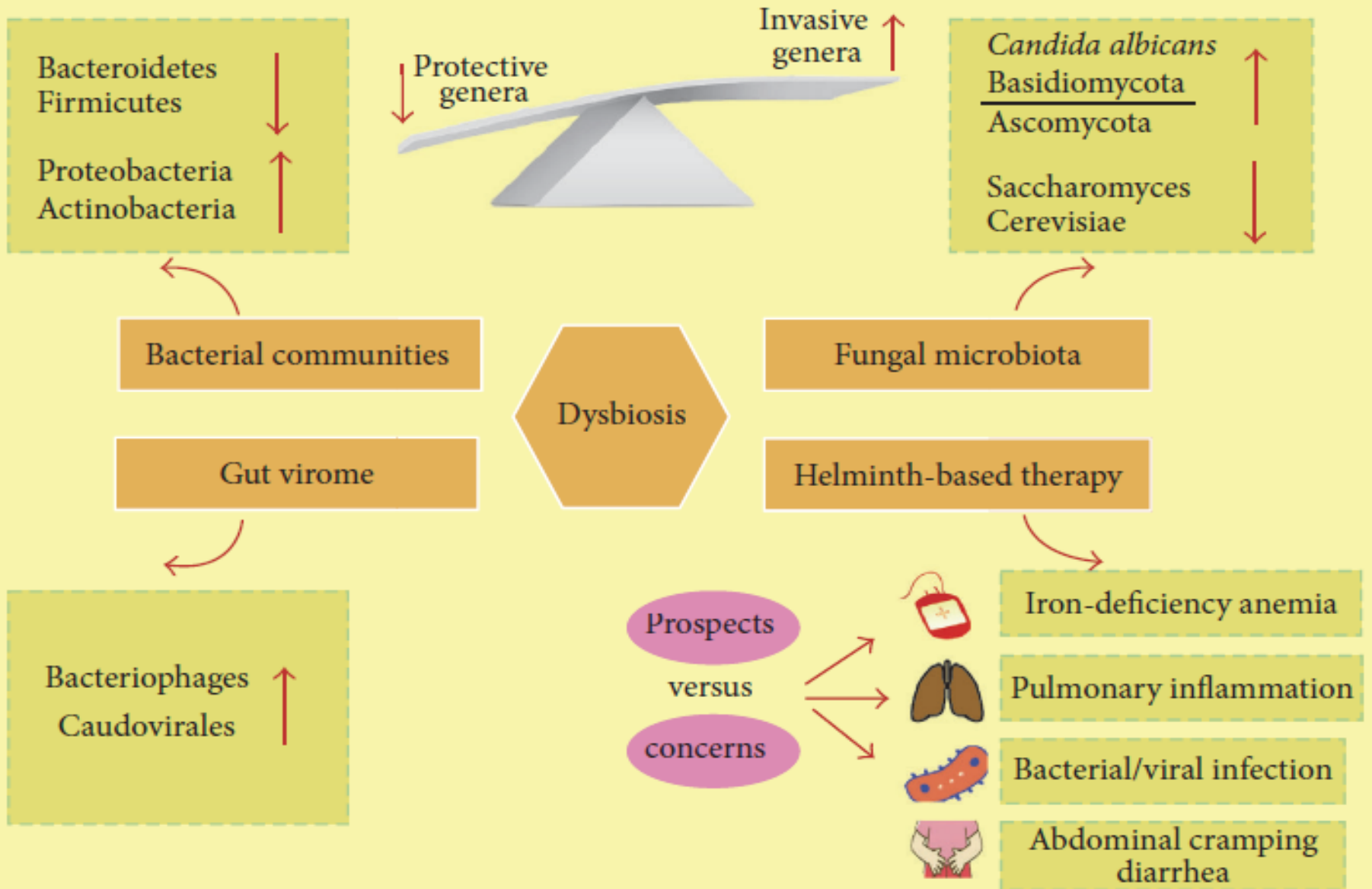
Vitamine D

- Effet anti-inflammatoire
- Manque de vitamine D dans env. 40% des patients MICI
- Population normales: manque de vitamine D dans env. 20%
- Impact clinique: chercher manque de Vit D et substituer si nécessaire

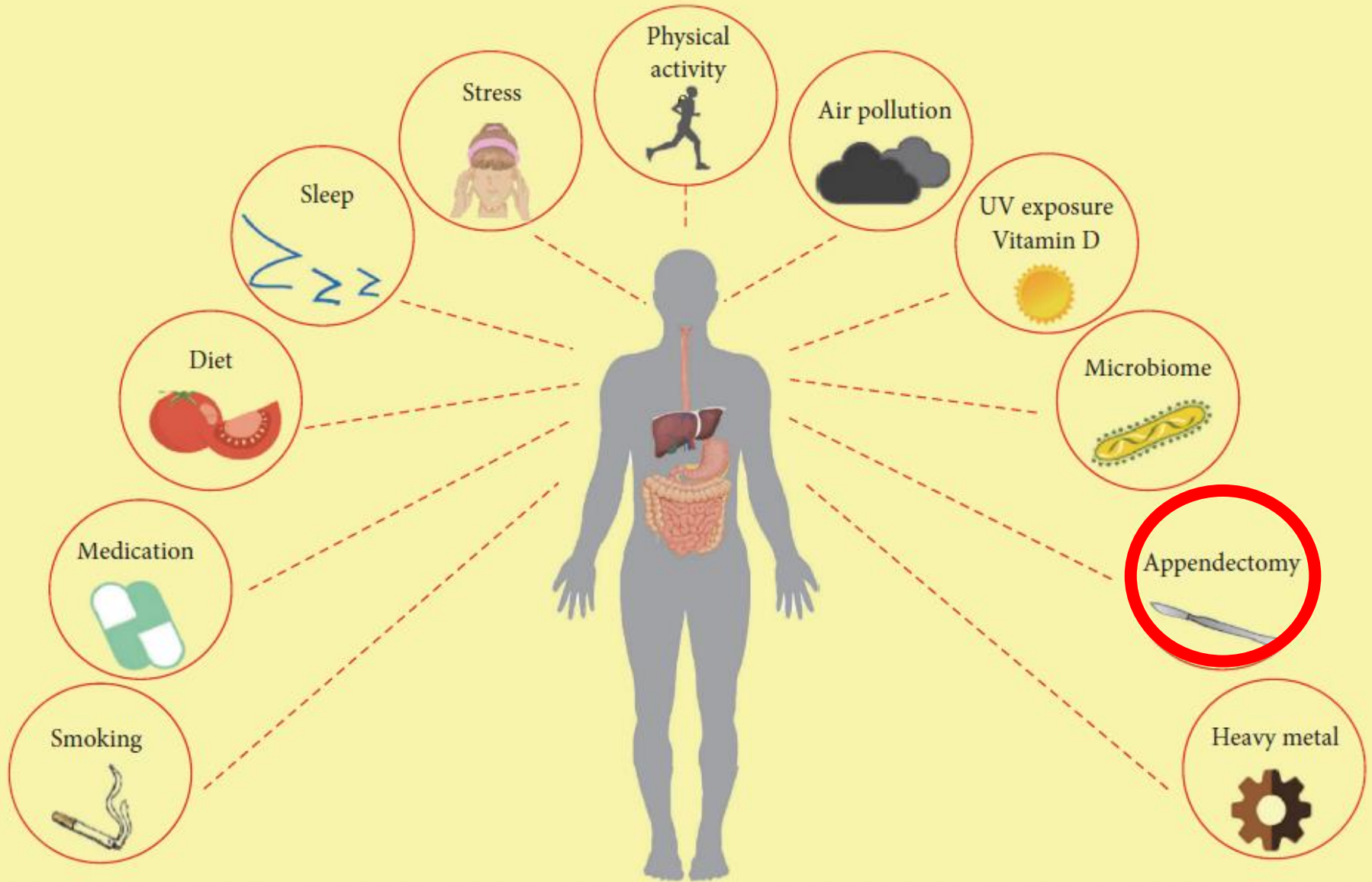
Environmental risk factors



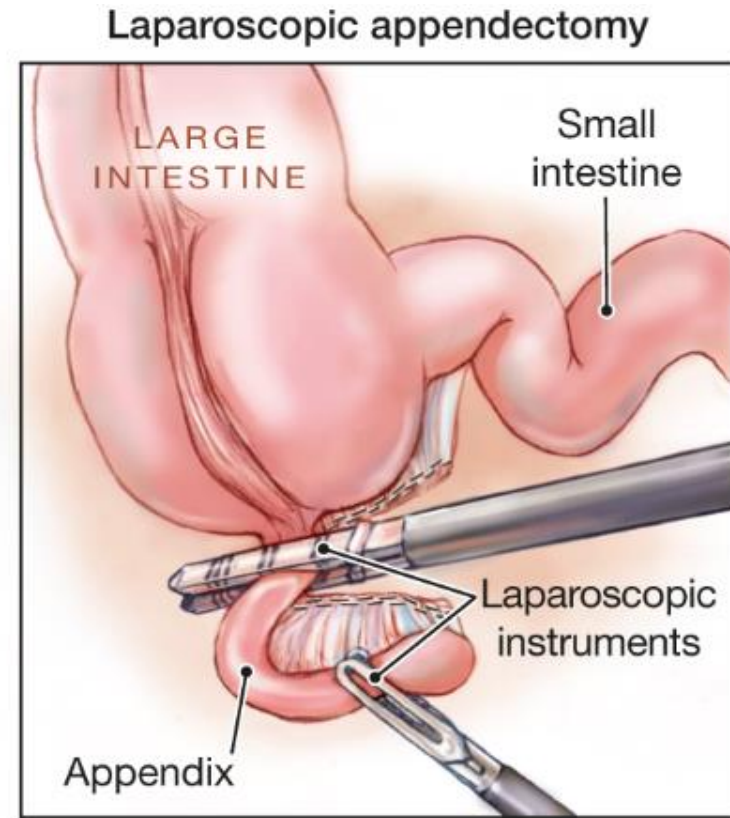
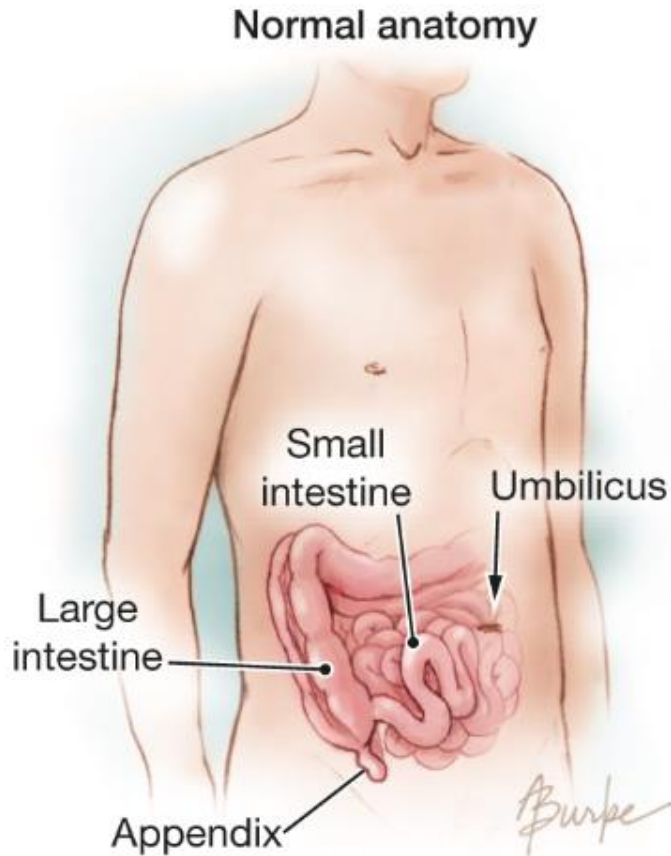
Dysbiosis



Environmental risk factors



Appendectomie



L'appendice est un organe immunologique

Appendectomy et MICI

Study Highlights

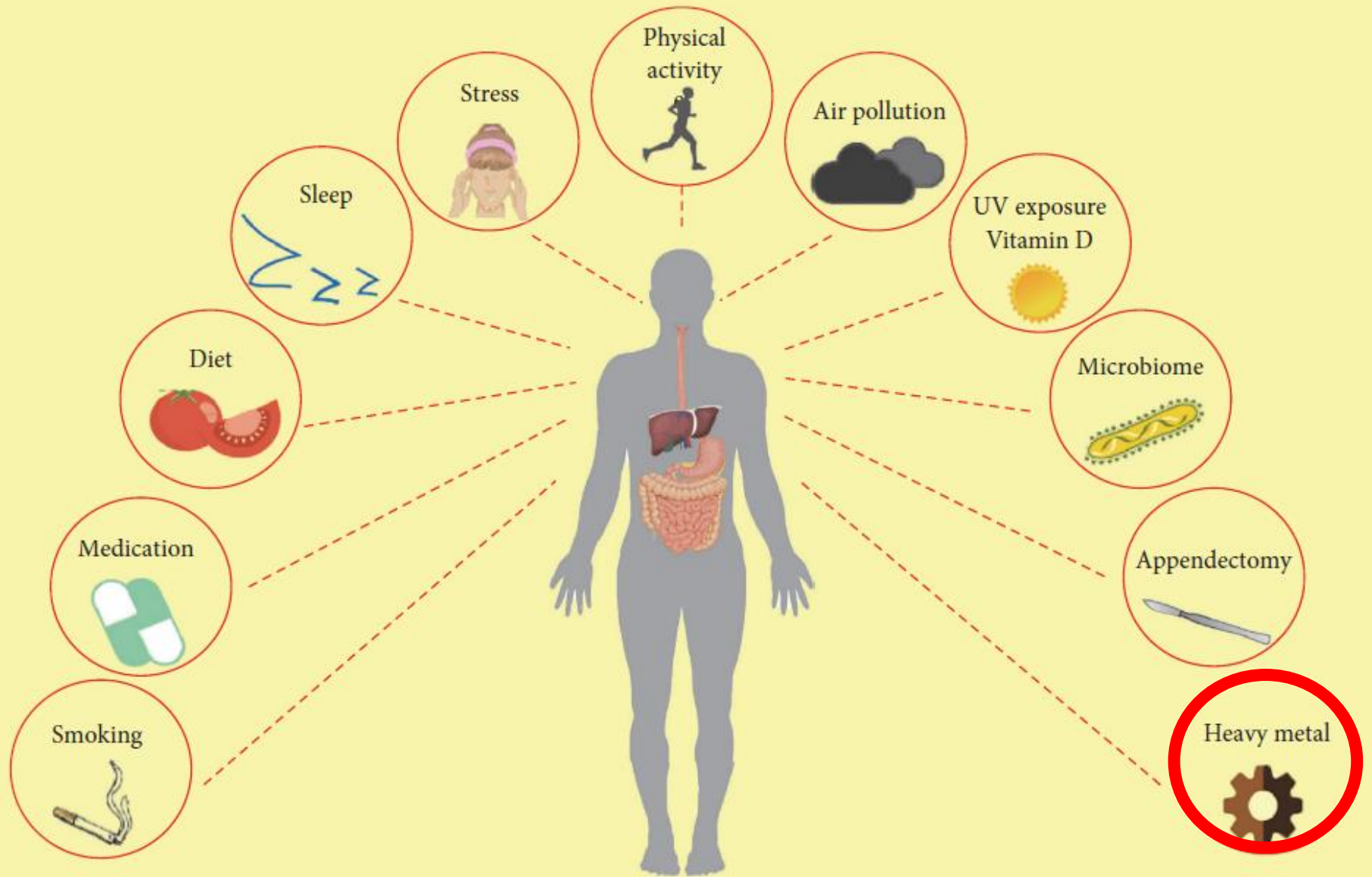
WHAT IS CURRENT KNOWLEDGE

- ✓ Appendectomy early in life due to an inflammatory condition is associated with a lower risk of developing ulcerative colitis (UC).

WHAT IS NEW HERE

- ✓ Appendectomy before UC for appendicitis before 20 years of age, and at any age for diagnoses other than appendicitis, is associated with a milder UC disease course with lower risk of colectomy.
- ✓ Appendectomy before UC diagnosis for appendicitis after 20 years of age does not affect the risk of colectomy.
- ✓ Appendectomy for appendicitis in established UC appears to be associated with a worse disease course with increased rate of subsequent colectomy.

Environmental risk factors



Micro-particles (TiO₂, SiO₂)

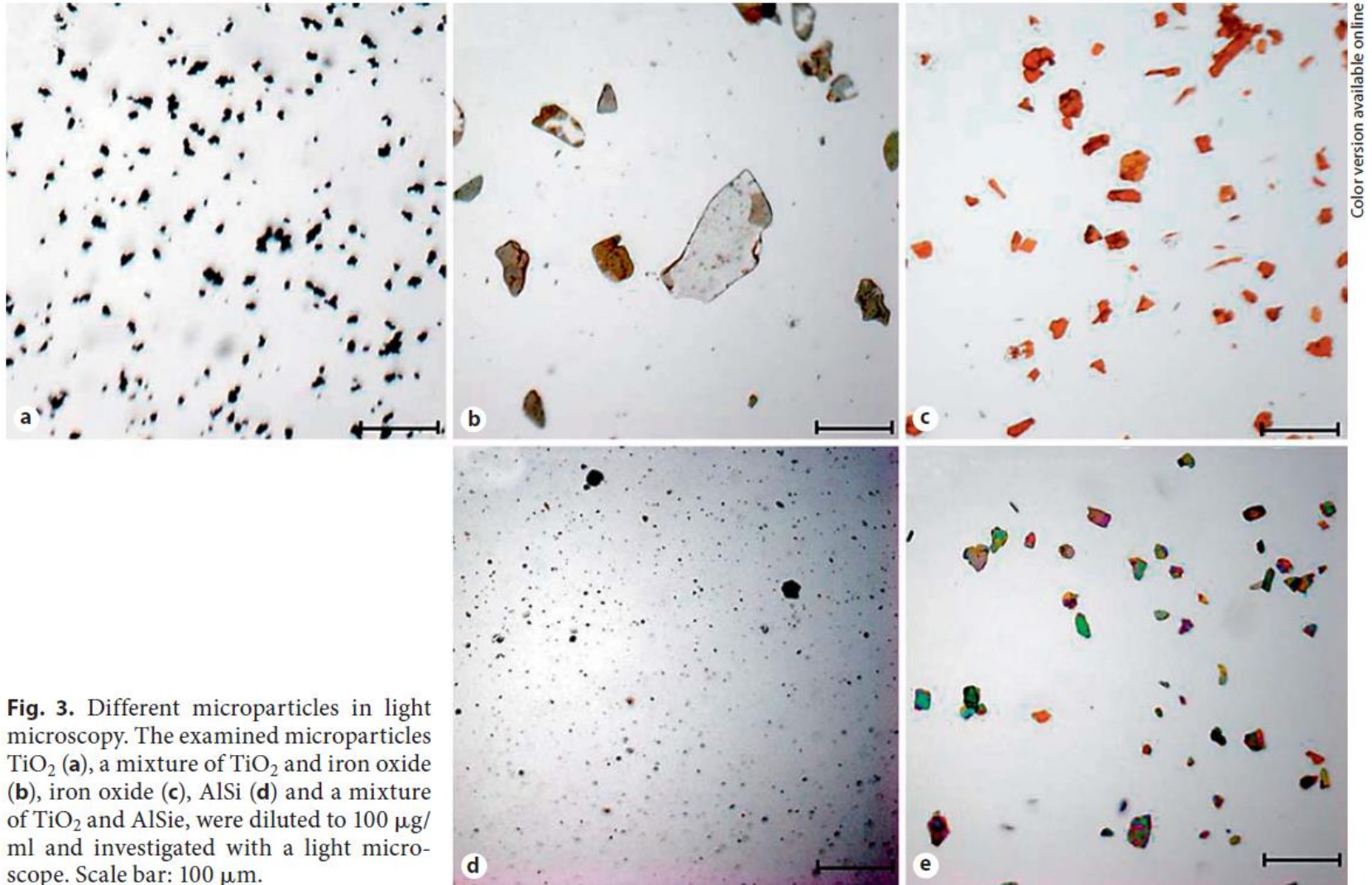


Fig. 3. Different micro-particles in light microscopy. The examined micro-particles TiO₂ (a), a mixture of TiO₂ and iron oxide (b), iron oxide (c), AlSi (d) and a mixture of TiO₂ and AlSi (e), were diluted to 100 µg/ml and investigated with a light microscope. Scale bar: 100 µm.

Table 2. Sources of microparticles in food products and estimated daily intake

Source	mg/person/day
TiO₂	
Food supplement tablet	37.5
Confectionary	24.4
Medicinal product tablet	15.0
Coffee whitener	0.52
Hard coated candies	0.32
Chewing gum	0.28
Marshmallows	0.27
Low-fat or fat-free dressings	0.22
AlSi	
Salt	1.30
Drinking chocolate powder	1.26
Chewing gum	0.92
Sugar, icing	0.30





OPEN ACCESS

ORIGINAL ARTICLE

Titanium dioxide nanoparticles exacerbate DSS-induced colitis: role of the NLRP3 inflammasome

Pedro A Ruiz,¹ Belen Morón,¹ Helen M Becker,¹ Silvia Lang,¹ Kirstin Atrott,¹ Marianne R Spalinger,¹ Michael Scharl,^{1,2} Kacper A Wojtal,¹ Anne Fischbeck-Terhalle,¹ Isabelle Frey-Wagner,¹ Martin Hausmann,¹ Thomas Kraemer,³ Gerhard Rogler^{1,2}

What is already known on this subject?

- ▶ Titanium dioxide induces reactive oxygen species (ROS) formation as well as inflammation in vitro and in vivo.
- ▶ The nucleotide-binding oligomerisation domain receptor, pyrin domain containing (NLRP3) inflammasome is activated in the presence of titanium dioxide.
- ▶ Polymorphisms in the *Nlrp3* gene have been linked to the development of Crohn's Disease.

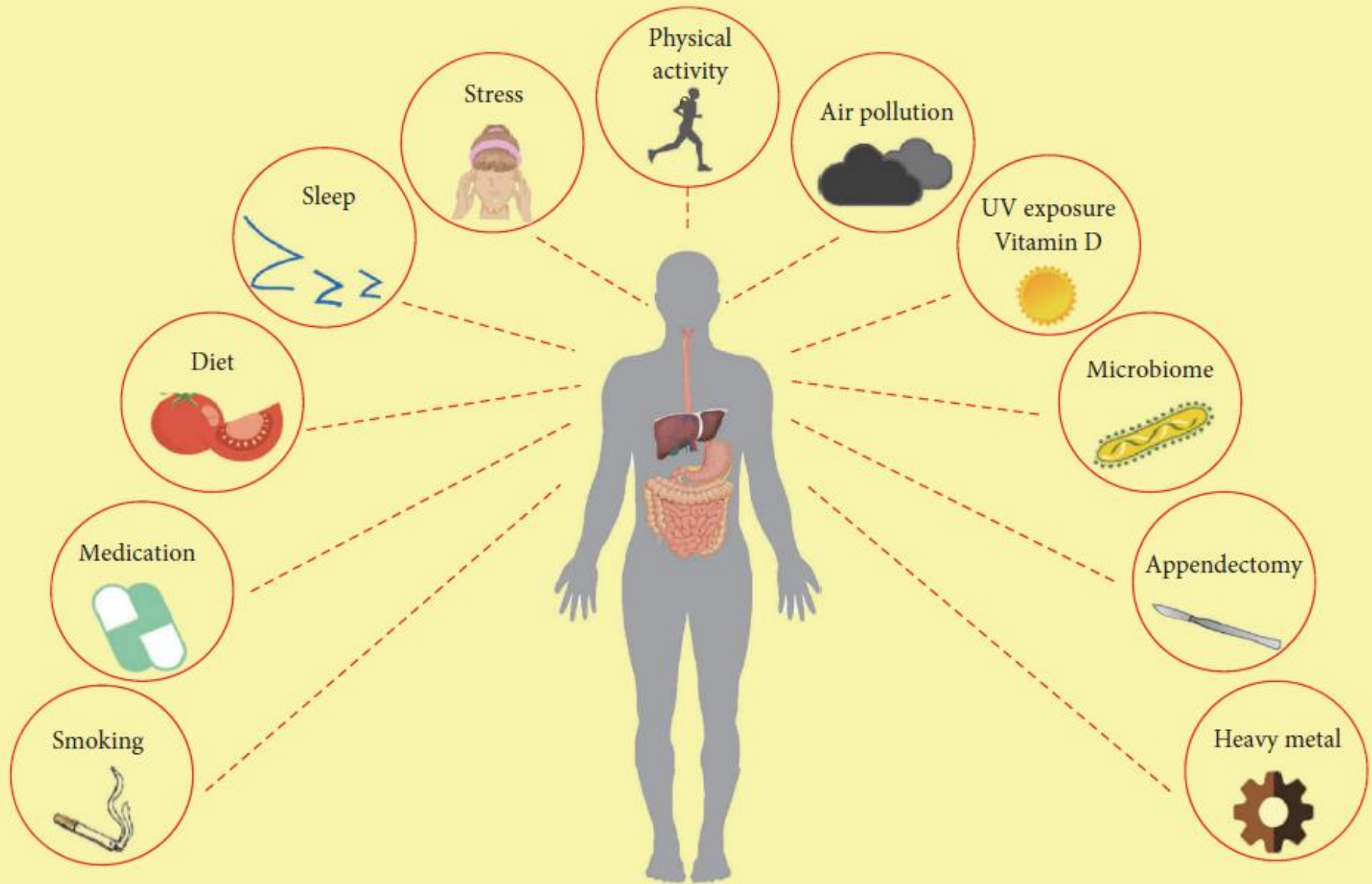
What are the new findings?

- ▶ Oral administration of titanium dioxide nanoparticles worsens intestinal inflammation in the dextran sodium sulfate (DSS) mouse model of colitis.
- ▶ Titanium dioxide crystals accumulate in the spleen of DSS-treated mice following oral gavage.
- ▶ Titanium dioxide particles accumulate and activate the NLRP3 inflammasome in human intestinal epithelial cells and macrophages.
- ▶ Levels of titanium are increased in the blood of patients with IBD.

How might it impact on clinical practice in the foreseeable future?

- ▶ Components of the inflammasome may represent novel therapeutic targets for the treatment of IBD.
- ▶ Our results suggest a cautionary use of titanium dioxide in pharmaceutical formulations and support a therapeutic benefit from low inorganic particle diet in patients with IBD.

Environmental risk factors



High Altitude Journeys and Flights are Associated with the Increased Risk of Flares in IBD Patients



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Maetzler², Benjamin
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 **Stadt Zürich**
Stadtspital Triemli

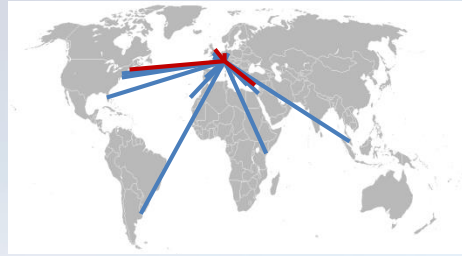
 **UniversitätsSpital
Zürich**

Résultats

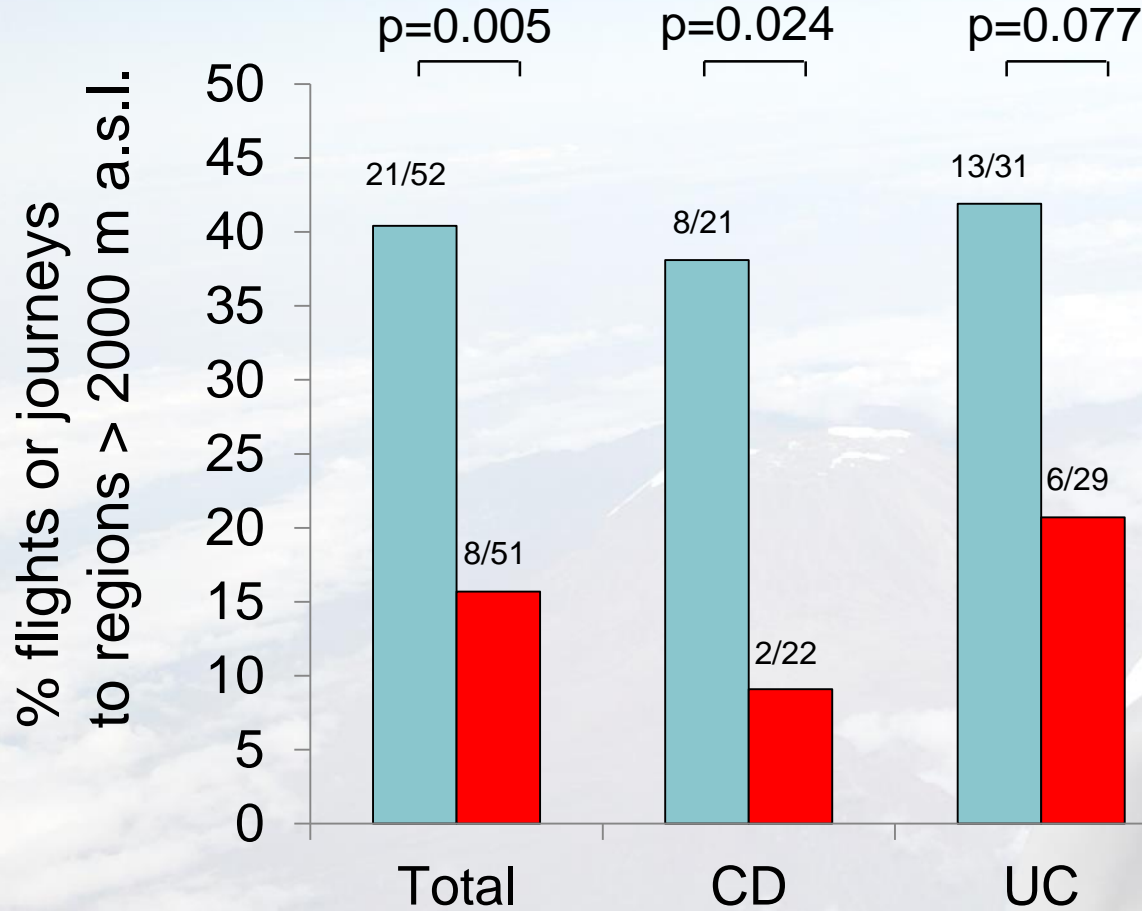
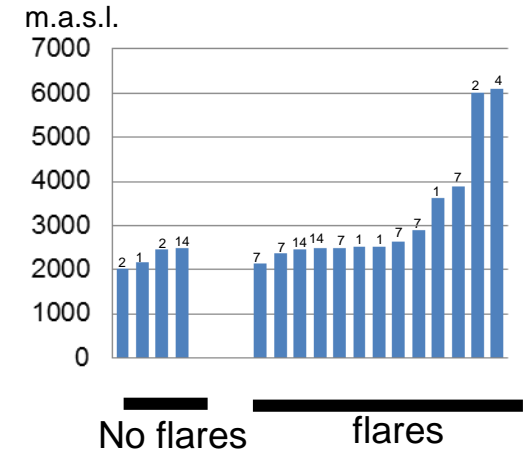
Total	103 IBD patients	
	43 M. Crohn	60 RCUH
	65% femmes	47% femmes
	39.3 ± 14.6 ans	43.1 ± 14.2 ans

**52 patients
Avec poussée
inflammatoire**

**51 patients
sans poussée
inflammatoire**

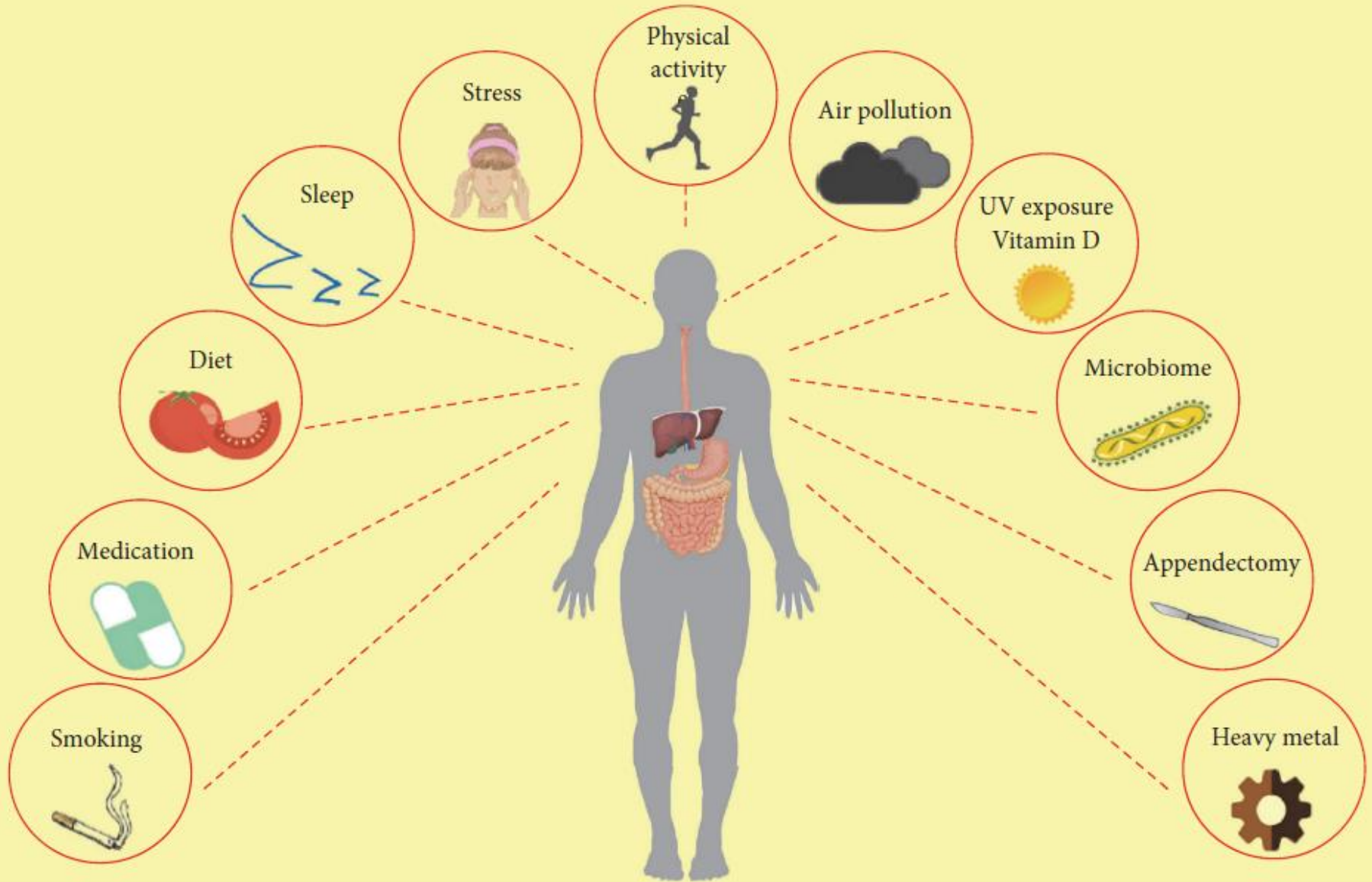


Résultats





Environmental risk factors



Vaccinations



Vaccination

History	Crohn's Disease	UC	All IBD
Ever vaccinated			
MMR	0.40 (0.08-2.00)	0.80 (0.18-3.56)	0.59 (0.21-1.69)
MCV	1.11 (0.26-4.69)	1.05 (0.20-5.42)	0.97 (0.34-2.79)
Unvaccinated	Reference	Reference	Reference

**All estimates shown are from conditional logistic regression, matched on health maintenance organization, sex, and birth year, and adjusted for race.*

Vaccination

History

Crohn's Disease

UC

All IBD

Les vaccins ne sont pas de facteur de risque pour le développement des MICI

health maintenance organization, sex, and birth year, and adjusted for race.

Merci !

