Clinique Saint-Luc
Bouge

Nouvelle approche diagnostic d'une infection urinaire

Julien Favresse

Plan

- Tigettes et sédiments urinaires
- Définition d'une infection urinaire
- Approche par statistiques « simples »
- Approches par statistiques « avancées » / machine learning

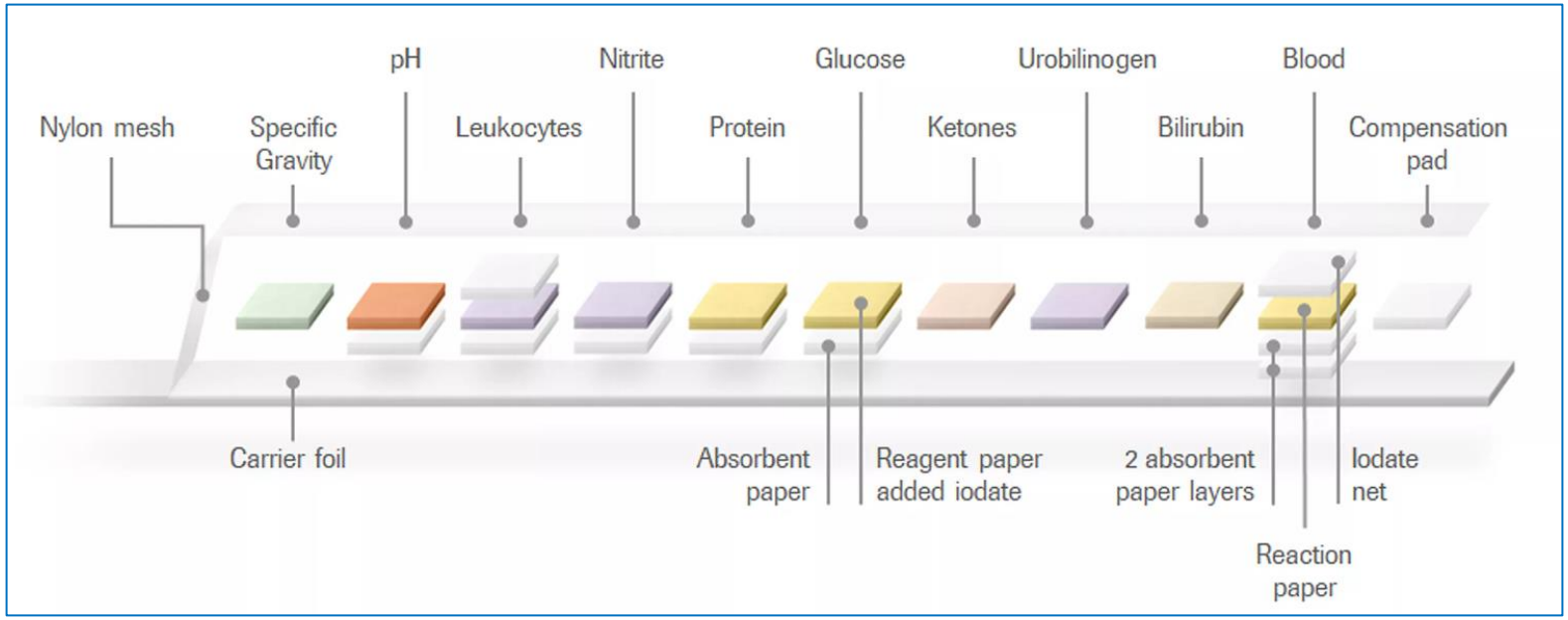
Tigette et sédiment urinaire

- **Tigette**
  - Nitrites
  - Leucocyte estérase
  - Corps cétoniques
  - Erythrocyte et hémoglobine
  - Glucose
  - Protéines
  - Bilirubine
  - Urobilinogène
  - pH
  - Densité
  - Couleur
  - Turbidité

- **Sédiment**
  - Globules blancs
  - Globules rouges
  - Cellules épithéliales
    - Squameuses
    - Non-squameuses
  - Cylindres
    - Pathologiques
    - Hyalins
  - Bactéries
  - Levures
  - Mucus
  - Cristaux

Tigette et sédiment urinaire

- **Tigette**
  - Urine absorbée sur des petits PAD
  - Réaction spécifique pour chaque analyte



Tigette et sédiment urinaire

- **Tigett**
  - Me
  - 5,5
  - Lun

5)

détecteur

A Photomètre a
B Zones réactiv
C Anneau de D

Tigette et sédiment urinaire

- **Tigette**
  - Réflectance # concentration de l'analyte dans l'urine
  - Très utile pour définir un test REFLEX quantitatif

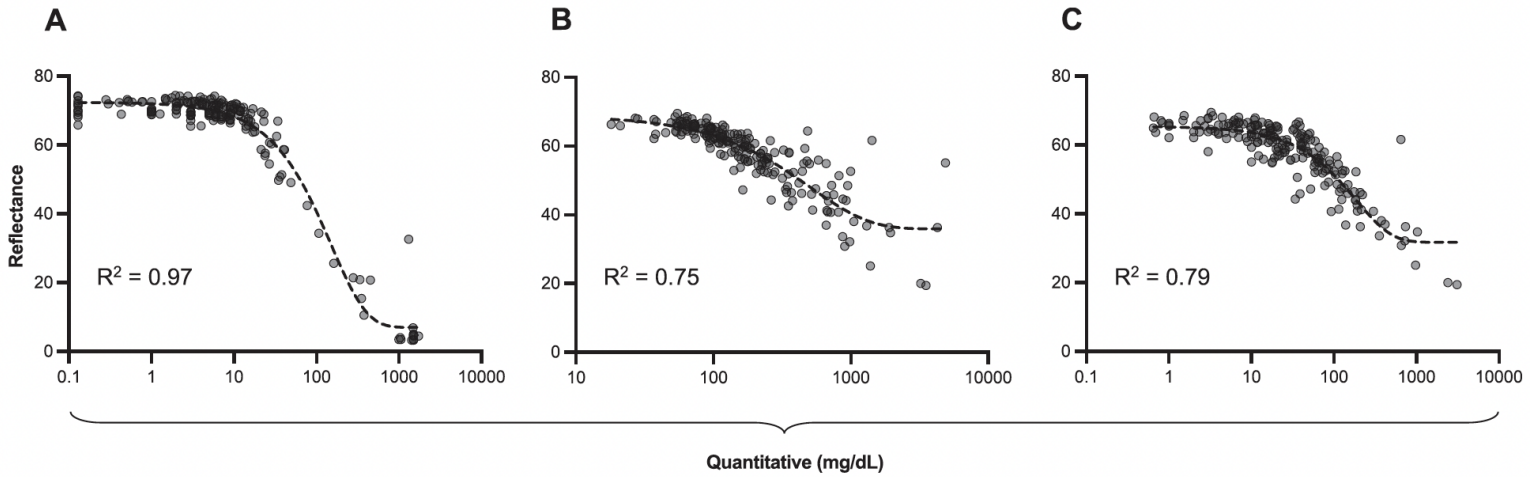
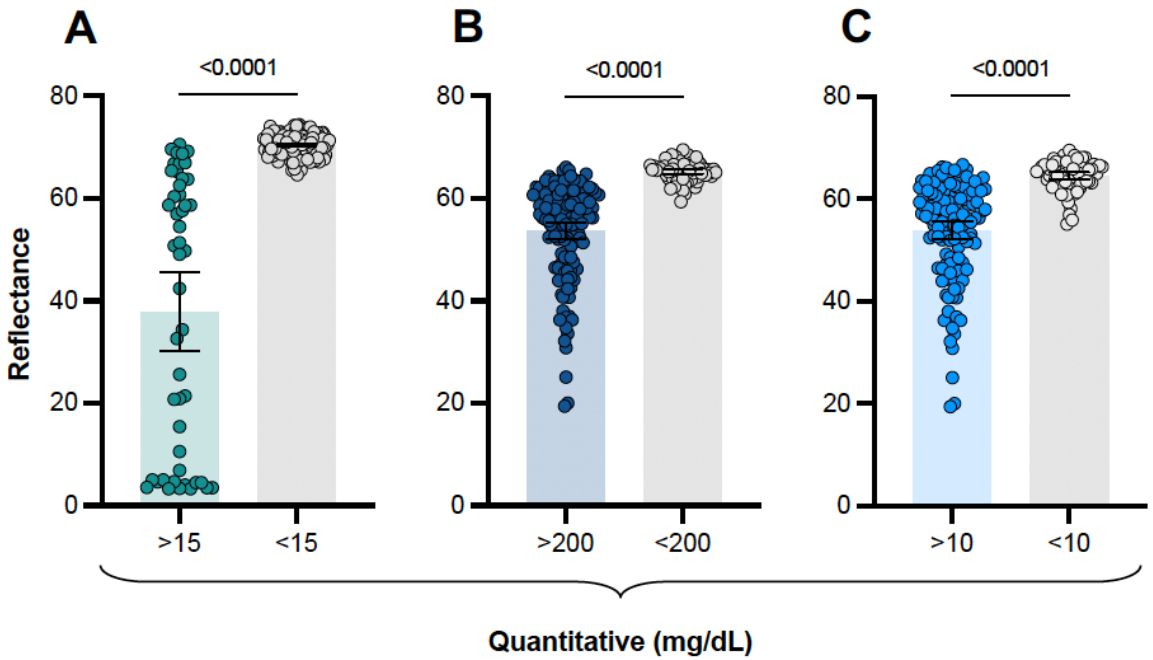


Fig. 2. Comparison of reflectance data to quantitative measurements. Correlation curves between reflectance data versus quantitative measurements. A = glucose; B = proteins; C = albumin.

Cabo and Favresse. Clinica Chimica Acta 2023. 10.1016/j.cca.2023.117534

Tigette et sédiment urinaire

- **Tigette**
  - Réflectance # concentration de l'analyte dans l'urine
  - Très utile pour définir un test REFLEX quantitatif



Cabo and Favresse. Clinica Chimica Acta 2023. 10.1016/j.cca.2023.117534

Tigette et sédiment urinaire

- **Tigette**
  - Réflectance # concentration de l'analyte dans l'urine
  - Très utile pour définir un test REFLEX quantitatif

		cobas 601 ordinal scale arbitrary concentrations	Menarini ordinal scale arbitrary concentrations	cobas 601 reflectance (optimized ROC curve)	cobas 601 reflectance (optimized for sensitivity)
Glucose > 15 mg/dL	FP_D	0.00	0.00	3.90	51.30
	FN_G	48.28	79.31	17.24	0.00
	FN_C	0.00	0.00	0.00	0.00
Glucose ≥ 54 mg/dL	FP_D	6.63	1.66	0.00	0.00
	FN_G	0.00	0.00	0.00	0.00
	FN_C	0.00	0.00	0.00	0.00
Proteins ≥ 200 mg/L	FP_D	22.66	1.56	13.28	58.59
	FN_G	4.55	31.82	4.55	0.00
	FN_C	9.09	0.00	10.00	0.00
Albumin ≥ 10 mg/L	FP_D	6.00	0.00	4.00	86.00
	FN_G	62.07	90.80	49.41	0.00
	FN_C	2.94	26.47	1.49	0.00

Cabo and Favresse. Clinica Chimica Acta 2023. 10.1016/j.cca.2023.117534

Tigette et sédiment urinaire

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- **Tigette**

Table 1
Comparison of sensitivity and specificity for glucose, proteins, and albumin using reflectance values versus ordinal scale arbitrary concentrations. Confidence intervals (95%) are represented in brackets. ROC: Receiver Operating Characteristic; AUC: Area Under the Curve; Se: Sensitivity; Sp: Specificity; PPV: Positive Predictive Value; NPV: Negative Predictive Value; NA: Not Applicable.

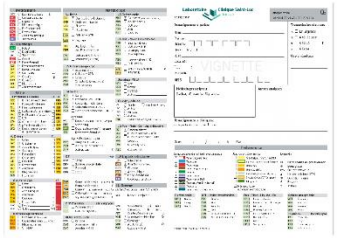
		cobas u 601 ordinal scale arbitrary concentrations	UC-MAX ordinal scale arbitrary concentrations	cobas u 601 reflectance (optimized ROC curve)	cobas u 601 reflectance (optimized for sensitivity)
Glucose > 15 mg/dL	Reflectance cut-off	NA	NA	≤ 66.96	≤ 70.57
	AUC	NA	NA	0.965 (0.929—0.985)	NA
	Se	71.4 (56.7—83.4)	53.1 (38.3—67.5)	89.8 (77.8—96.6)	100 (92.7—100)
	Sp	100 (97.7—100)	100 (97.7—100)	96.1 (91.7—98.6)	48.7 (40.6—56.9)
	PPV	100	100	87.9 (76.8—94.1)	38.13 (34.6—41.8)
	NPV	91.7 (87.7—94.5)	87.1 (83.3—90.1)	96.8 (92.8—98.6)	100
	Accuracy	93.1 (88.8—96.2)	88.7 (83.6—92.7)	94.6 (90.5—97.3)	61.0 (54.0—67.8)
Glucose > 54 mg/dL	Reflectance cut-off	NA	NA	≤ 42.42	≤ 42.42
	AUC	NA	NA	1.000 (0.982—1.000)	1.000 (0.982—1.000)
	Se	65.7 (47.8—80.9)	100 (85.2—100)	100 (85.2—100)	100.00 (85.2—100.0)
	Sp	100 (97.84—100)	98.3 (95.2—99.7)	100 (98.0—100)	100 (98.0—100)
	PPV	100	88.5 (71.4—95.9)	100	100
	NPV	95.8 (93.6—97.3)	100	100	100
	Accuracy	96.1 (92.5—98.3)	98.5 (95.8—99.7)	100 (98.2—100)	100 (98.2—100)
Proteins ≥ 200 mg/L	Reflectance cut-off	NA	NA	≤ 59.33	≤ 64.38
	AUC	NA	NA	0.959 (0.923—0.982)	NA
	Se	94.8 (87.2—98.6)	72.7 (61.4—82.3)	94.7 (87.1—98.5)	100 (95.3—100)
	Sp	77.3 (69.1—84.3)	98.4 (94.5—99.8)	86.7 (79.6—92.1)	41.41 (32.8—50.4)
	PPV	71.6 (64.5—77.7)	96.6 (87.6—99.1)	81.1 (73.3—87.0)	50.7 (47.0—54.3)
	NPV	96.1 (90.5—98.5)	85.7 (80.6—89.6)	96.5 (91.3—98.6)	100
	Accuracy	83.9 (78.1—88.7)	88.8 (83.6—92.8)	89.7 (84.7—93.5)	63.4 (56.4—70.0)
Albumin ≥ 10 mg/L	Reflectance cut-off	NA	NA	≤ 61.89	≤ 67.91
	AUC	NA	NA	0.900 (0.850—0.937)	NA
	Se	63.9 (55.8—71.4)	36.9 (29.4—45.0)	72.1 (64.3—79.0)	100 (97.6—100)
	Sp	94.0 (83.5—98.8)	100 (92.6—100)	96.0 (86.3—99.5)	14.0 (5.8—26.7)
	PPV	97.0 (91.6—99.0)	100	98.2 (93.3—99.5)	78.2 (76.2—80.0)
	NPV	45.8 (40.4—51.3)	34.0 (31.4—36.7)	52.3 (45.9—58.6)	100
	Accuracy	71.3 (64.5—77.4)	52.4 (45.3—59.4)	77.6 (71.2—83.1)	78.9 (72.7—84.3)

Cabo and Favresse. Clinica Chimica Acta 2023. 10.1016/j.cca.2023.117534

Flux des urines (1)

- **Tigette**

1.



2.

3.

4.

5.

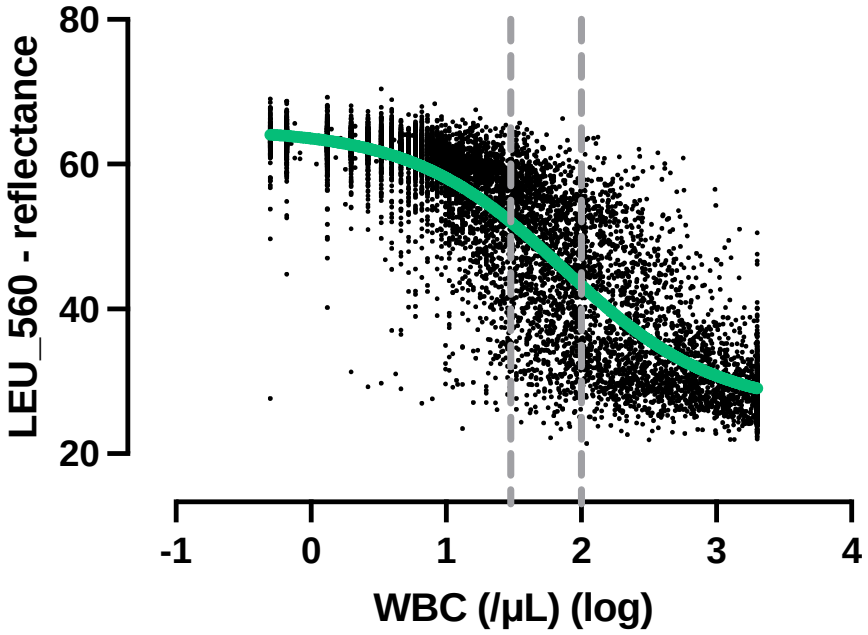
6.

Dosage quantitatif
- Protéines
- Glucose

7.

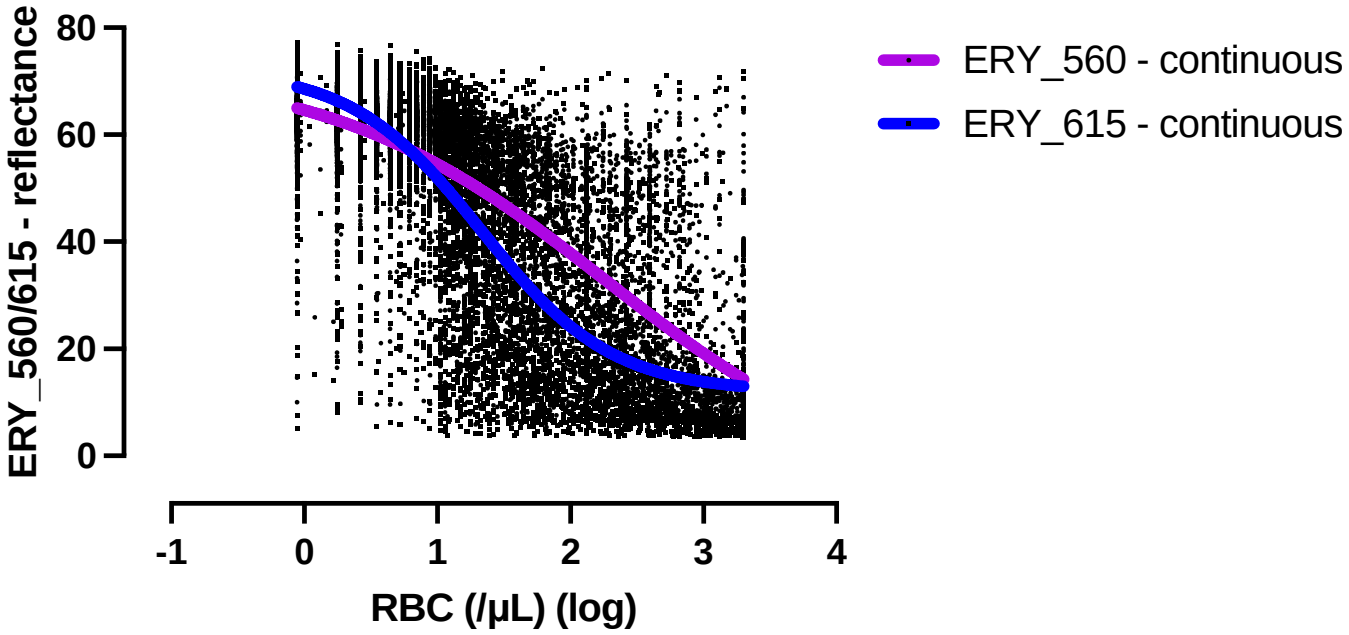
Tigette et sédiment urinaire

- **Tigette**
  - Réflectance # concentration de l'analyte dans l'urine
  - Très utile pour définir un test REFLEX quantitatif



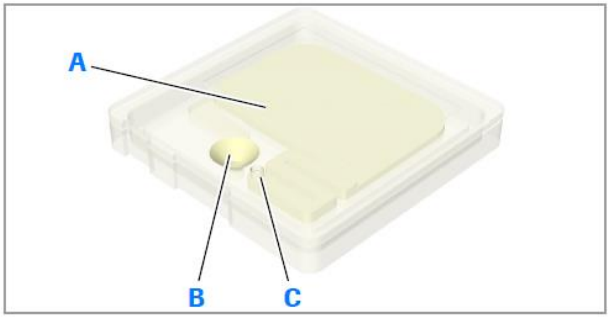
Tigette et sédiment urinaire

- **Tigette**
  - Réflectance # concentration de l'analyte dans l'urine
  - Très utile pour définir un test REFLEX quantitatif

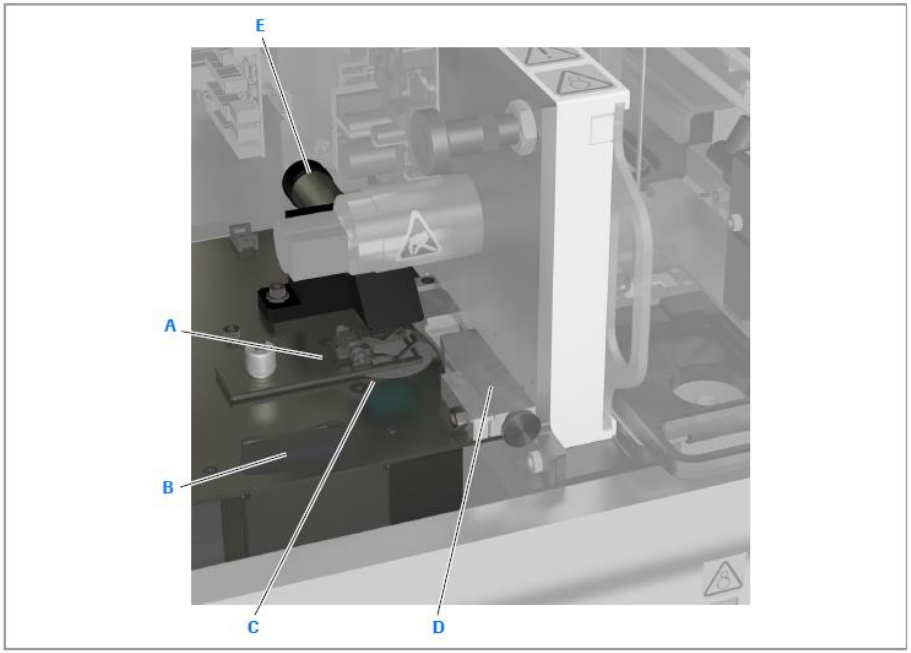


Tigette et sédiment urinaire

- **Sédiment**
  - Cuvette avec lecture au microscope digital
  - Eléments rassemblés en une seule couche



A Zone photographique, contient l'urine
B Orifice d'injection
C Zone de débordement



A Bras du microscope
B Dévidoir à déchets
C Support microscope
D Rail cuvettes
E Lampe du microscope

Tigette et sédiment urinaire

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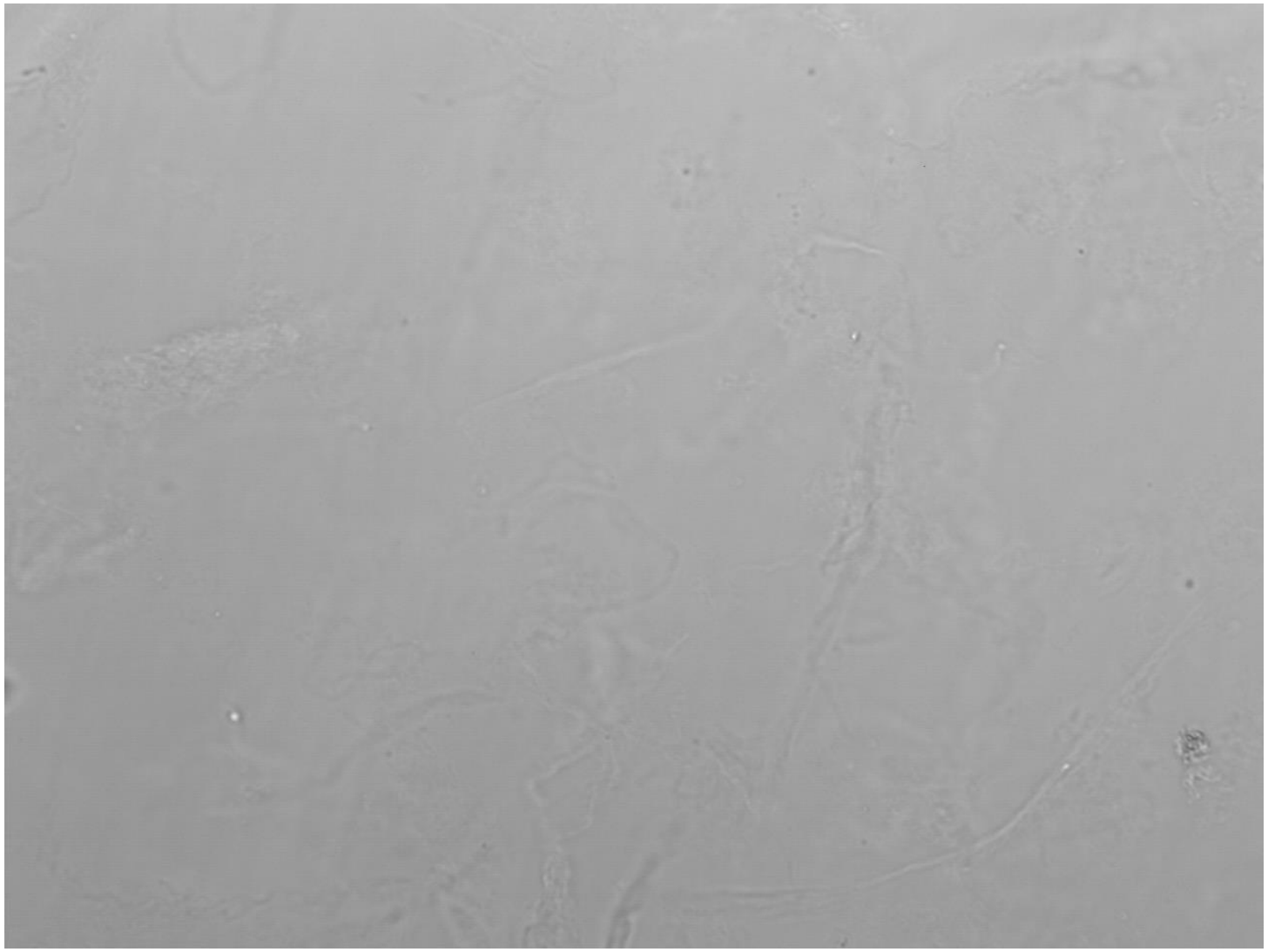
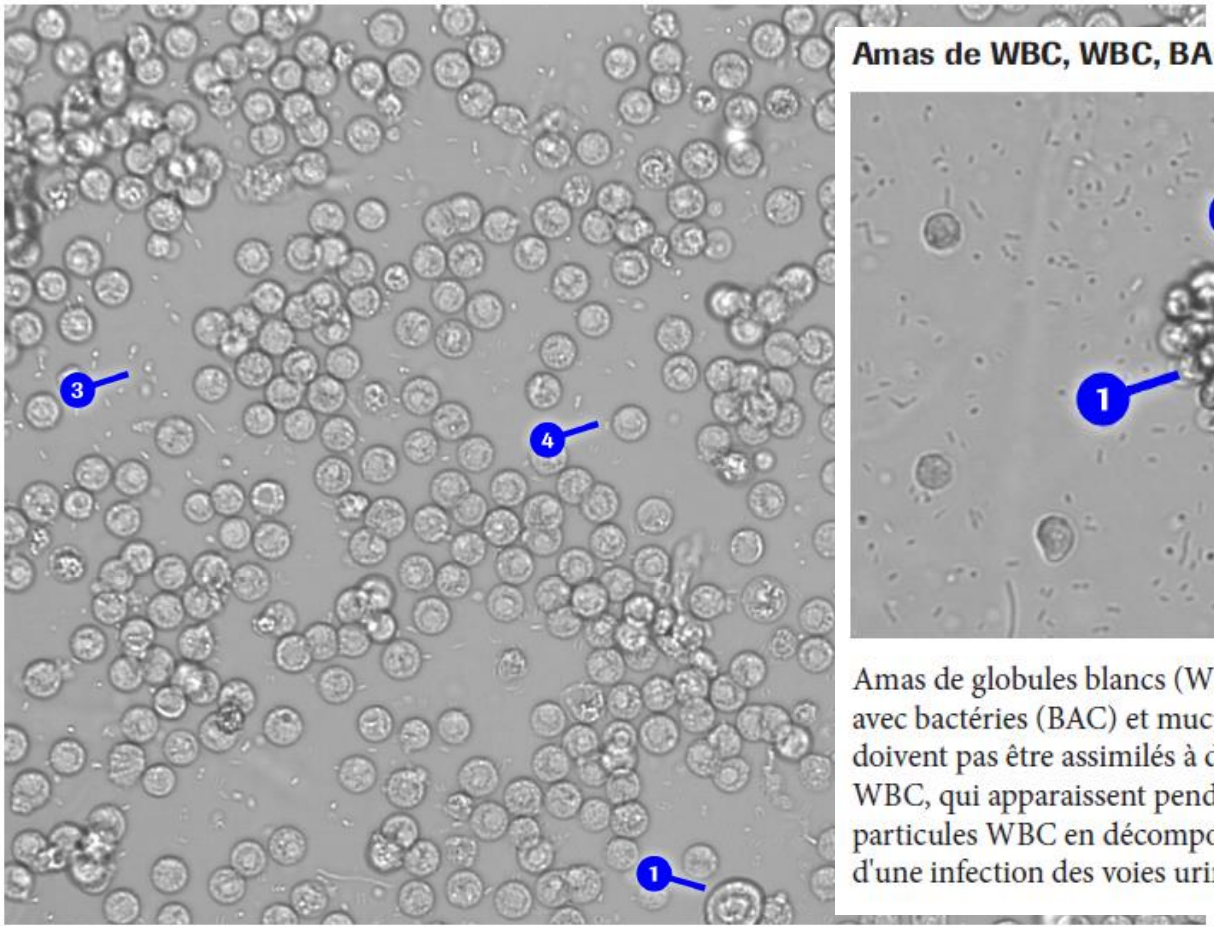
- **Sédiment** (négatif)



Tigette et sédiment urinaire

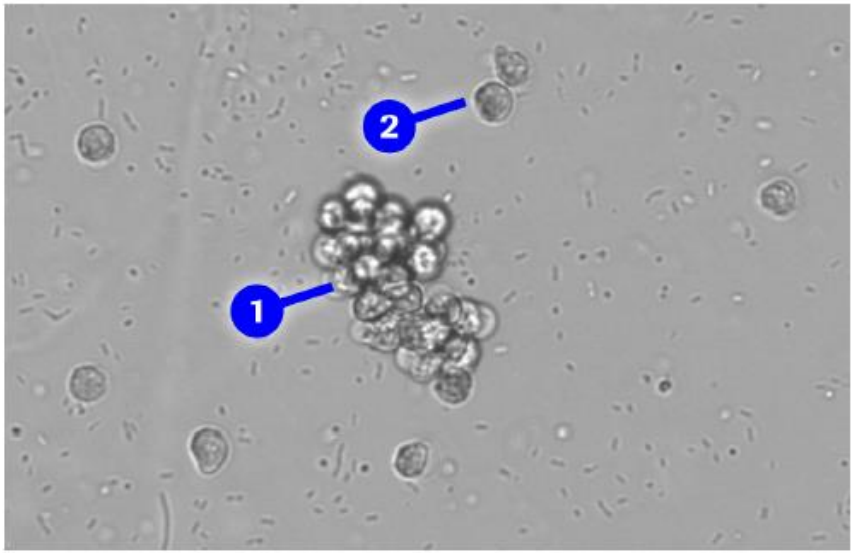
- **Sédiment** (GB)

WBC, RBC, NEC et BAC



Cellule épithéliale non squameuse (NEC) (1), quelques globules rouges (RBC) (2) et quelques bactéries (BAC) (3), en plus de nombreux globules blancs (WBC) (4). Les neutrophiles polymorphonucléaires (12 – 15 µm) sont aisément reconnaissables par leur noyau segmenté.

Amas de WBC, WBC, BAC et MUC



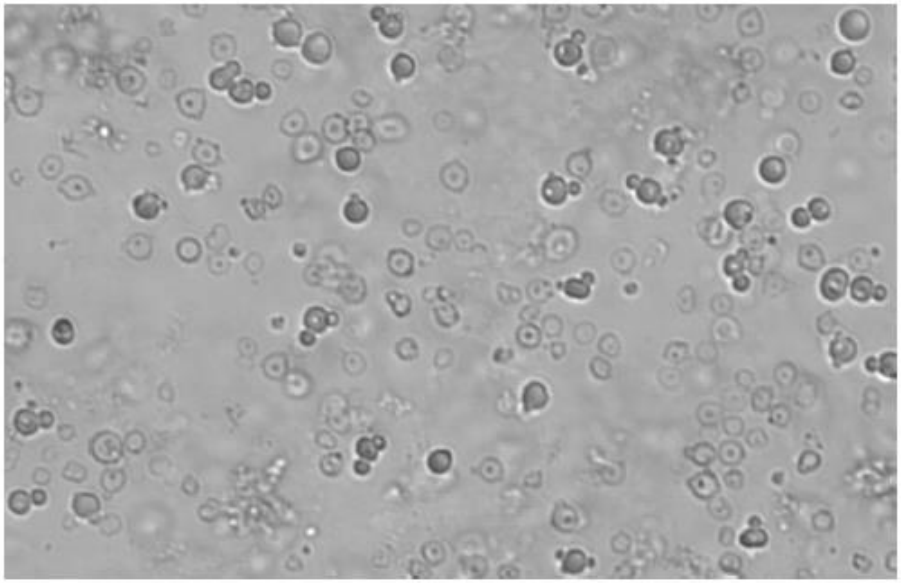
Amas de globules blancs (WBC) (1), globules blancs (WBC) (2) avec bactéries (BAC) et mucus (MUC). Les amas de WBC ne doivent pas être assimilés à des cylindres de WBC. Ces amas de WBC, qui apparaissent pendant la phagocytose des BAC et des particules WBC en décomposition, surviennent typiquement lors d'une infection des voies urinaires (UTI).

Tigette et sédiment urinaire

- **Sédiment** (GR iso/dysmorphiques)

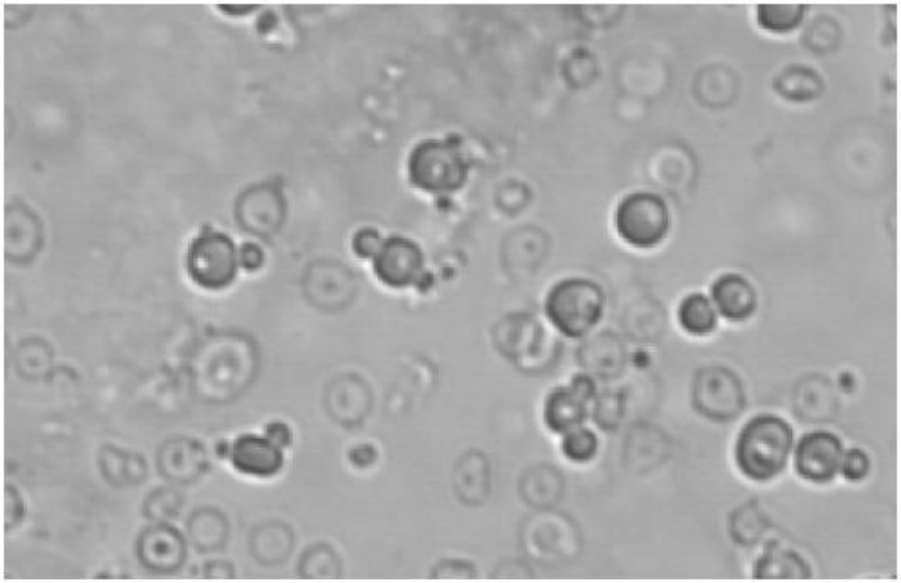
RBC

RBC



Globules rouges dismorphiques (désignés par RBC). Les RBC dits « dysmorphiques » ont subi des changements morphologiques dans les reins (cellules glomérulaires). Les acanthocytes (décrits comme des RBC) sont considérés comme d'origine presque exclusivement glomérulaire.

RBC, grossissement de 200 %



Globules rouges dismorphiques (désignés par RBC). Les RBC présentant diverses lésions membranaires (perte de cytoplasme, extrusion cytoplasmique de la membrane cellulaire, éléments granulaires sur la membrane cellulaire, etc.).

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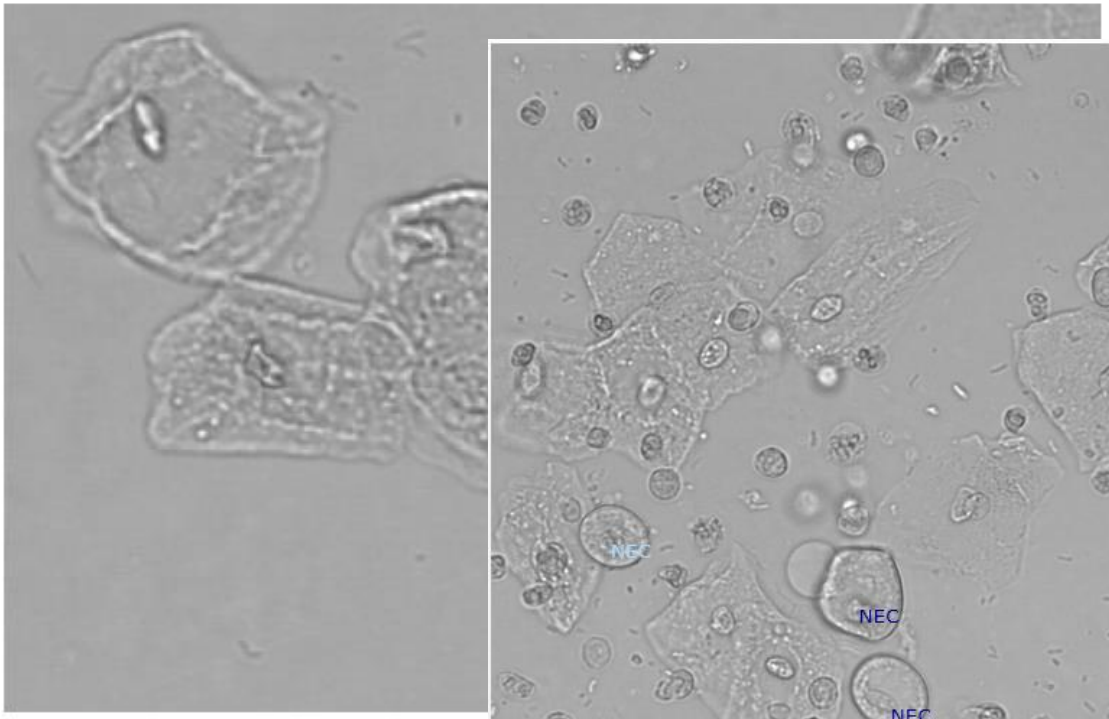
- **Sédiment** (SEC et NEC)

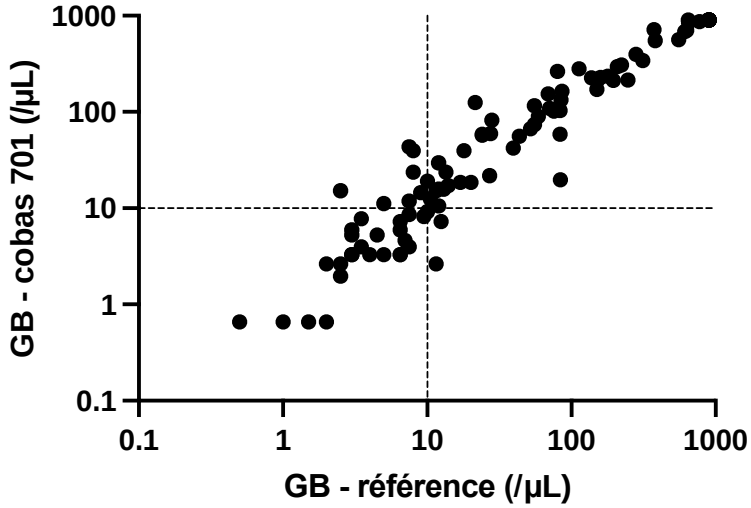
SEC



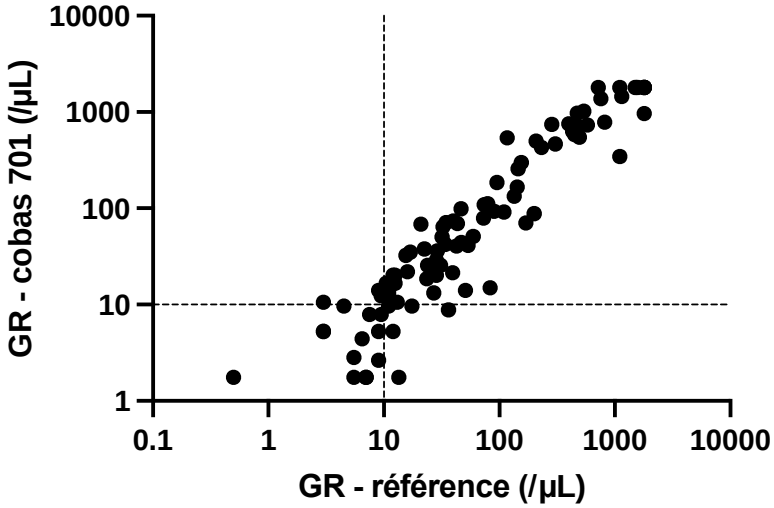
Les cellules épithéliales squar
grosses du sédiment urinaire
tiers distal de l'urètre chez l'h
chez la femme.

- **Sédiment (manuel versus automatique)**

Pearson r = 0.98
Spearman r = 0.96



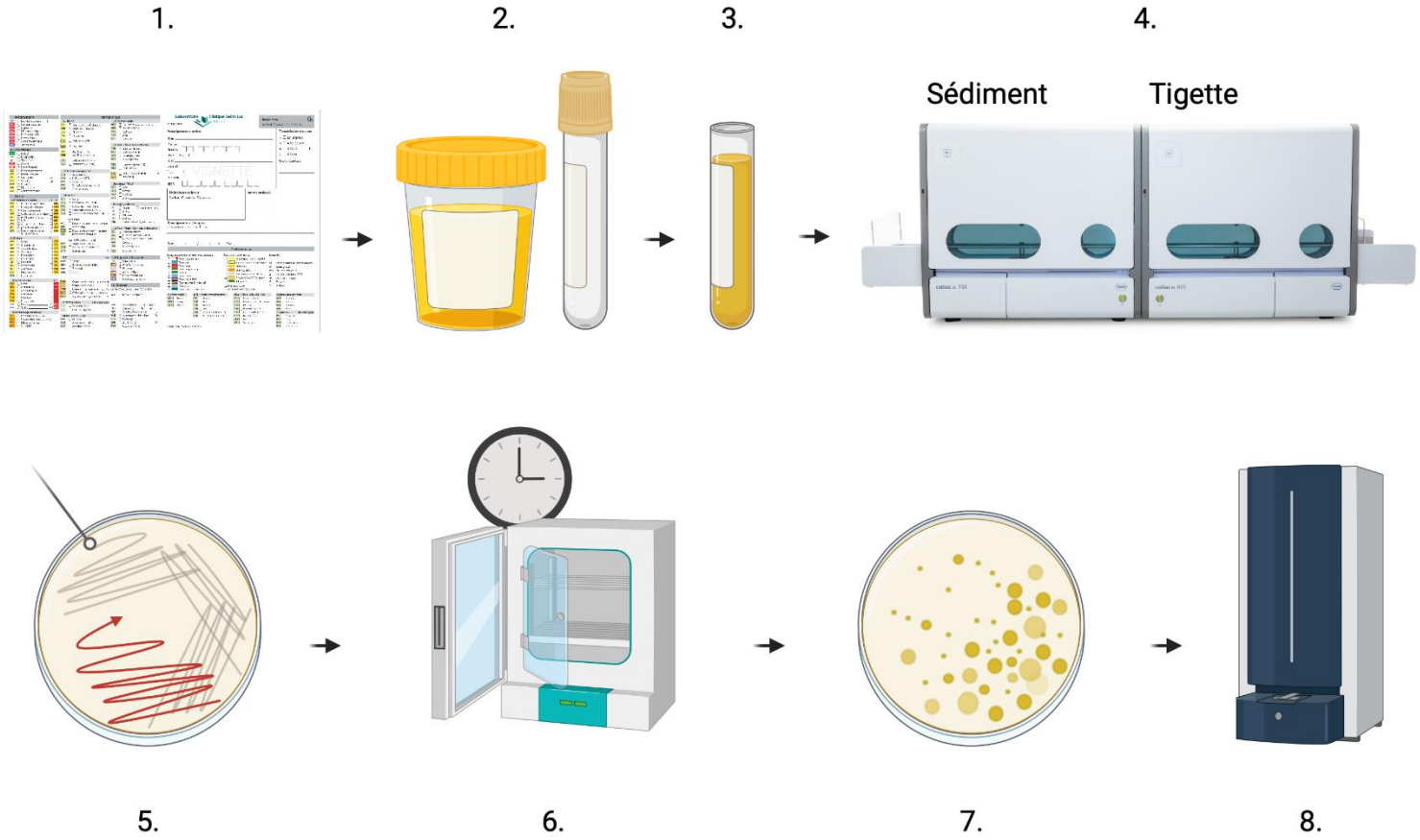
Pearson r = 0.93
Spearman r = 0.94



- 2 lecteurs indépendants au microscope (cellule de comptage uriglass)
- Comptage cobas 701
- 100 urines fraiches
- Critère EFLM = Spearman r >0.9

Flux des urines (2)

- **Sédiment**



Délai de 24-48h pour identifier le germe impliqué!

Flux des urines (2)

- **Protocole**

	Cas #1	**Cas #2**
Tigette/sédiment	- Femme - 37 ans - NIT + - LEU +++ - GB 172/µL	- Femme - 41 ans - NIT + - LEU +++ - GB 160/µL
Microbiologie	**Culture négative**	***E. coli* CFU >10^5/mL**

Infection urinaire

- Définition d'une infection urinaire?
  - Culture
    - Germe(s) identifié(s)?
    - Quantité? CFU
    - Pure? Mixte? Prédominance?
    - Présence de globules blancs?

Infection urinaire

- Définition d'une infection urinaire?

Etude	Critère
Heckerling *et al.* 2007 IJMI	(1) $\geqq 10^5$ CFU/mL et si uropathogène ou (1') $\geqq 10^2$ CFU/mL et si uropathogène
Sterry-Blunt *et al.* 2015 JMM	(1) $\geqq 10^4$ CFU/mL. *NB: flore mixte considérée comme négative*
Shimoni et al. 2017 Plos One	(1) $\geqq 10^5$ CFU/mL, any bacteria
Taylor *et al.* 2018 PloS One	(1) $>10^4$ CFU/HPF (2) flore mixte si *E. coli* présent
De la Tabla *et al.* 2019 Ann Clin Chem	(1) $\geqq 10^4$ CFU/mL. *NB: $\geqq$3 isolats = contamination*
Burton *et al.* 2019 BMC MIDM	(1) Tous les isolats avec ATBG associé. *NB: flore mixte considérée comme négative*
Dedeene *et al.* 2023 RBSLM poster	(1) $\geqq 10^4$ CFU/mL et si uropathogène. *NB: flore mixte considérée comme négative*

Infection urinaire

- Définition d'une infection urinaire?

Open Forum Infectious Diseases

REVIEW ARTICLE

Definitions of Urinary Tract Infection in Current Research: A Systematic Review

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Defining urinary tract infection (UTI) is complex, as numerous clinical and diagnostic parameters are involved. In this systematic review, we aimed to gain insight into how UTI is defined across current studies. We included 47 studies, published between January 2019 and May 2022, investigating therapeutic or prophylactic interventions in adult patients with UTI. Signs and symptoms, pyuria, and a positive urine culture were required in 85%, 28%, and 55% of study definitions, respectively. Five studies (11%) required all 3 categories for the diagnosis of UTI. Thresholds for significant bacteriuria varied from 10^3 to 10^5 colony-forming units/mL. None of the 12 studies including acute cystitis and 2 of 12 (17%) defining acute pyelonephritis used identical definitions. Complicated UTI was defined by both host factors and systemic involvement in 9 of 14 (64%) studies. In conclusion, UTI definitions are heterogeneous across recent studies, highlighting the need for a consensus-based, research reference standard for UTI.

Keywords. complicated urinary tract infection; cystitis; definition; pyelonephritis; urinary tract infection.

Infection urinaire

- Définition d'une infection urinaire?

Table 7-3. The pathogenicity and frequency of example microorganisms in urine

		Frequency (percent of isolates)			
Pathogenicity in the urinary tract		**uUTI**	**cUTI**	**HA-UTI**	**CA-UTI**
I. Primary pathogens	*E. coli*	70-75	55-65	45	30
	S. saprophyticus	3-6	-	-	-
II. Secondary pathogens	*Enterobacter* spp.	2	4	6	3
	Enterococcus spp.	4-5	6-11	10	10
	Klebsiella spp.	5-6	8-9	12	5
	Proteus spp.	2-4	2-5	6	11
	P. aeruginosa	1-3	2-7	9	11
	S. aureus	1-2	2-3	3	4
	Citrobacter spp.	2	3	1.5	5
	M. morganii	<1	5	<1	4
	Serratia spp.	<1	7	<1	<1
	Aerococcus spp.	1	1	-	-
	Actinotignum schaalii	<0.1	<0.1	-	-
	C. urealyticum	-	-	-	-
III. Doubtful pathogens	*Streptococcus agalactiae*	3-4	2-3	<1	<1
	Yeast	1	3-7	2	7
	Acinetobacter spp.	<1	2	2	2
IV. Contaminants	*Staphylococcus*, coagulase negative (except *S. saprophyticus*) *Corynebacterium* spp (except *C. urealyticum*) *Gardnerella vaginalis* *Lactobacillus* spp. (except *L. delbrueckii*)				

Abbreviations used: uUTI, uncomplicated urinary tract infection; cUTI, complicated urinary tract infection; HA-UTI, healthcare-associated urinary tract infection; CA-UTI, catheter-associated urinary tract infection; - , no data available.

EFLM Guidelines 2023

Infection urinaire

Clinique Saint-Luc Bouge

- Définition d'une infection urinaire?

Définition 1	Définition 2	Définition 3	Définition 4	Définition 5
European association of urology 2015	**Public Health England (PHE)/Health Protection Agency guidelines**	**POETIC protocol**	**EFLM (1)**	**EFLM (2)**
≧10^3 CFU/mL uropathogène	≧10^5 CFU/mL uropathogène (prédominance dans flore mixe)	≧10^5 CFU/mL uropathogène (pure)	≧10^3 CFU/mL pathogène classe 1 + GB ≧30	≧10^3 CFU/mL pathogène classe 1 + GB ≧30
	≧10^4 CFU/mL uropathogène (pure)	>10^4 et <10^5 CFU/mL uropathogène (pure) + GB ≧30	≧10^4 CFU/mL pathogène classe 2 + GB ≧30	≧10^4 CFU/mL pathogène classe 2 + GB ≧30
	≧10^3 CFU/mL, *E. coli* ou *S. saprophyticus*	≧10^5 CFU/mL uropathogène (prédominance dans flore mixe)	≧10^5 CFU/mL pathogène classe 3 + GB ≧30	≧10^5 CFU/mL pathogène classe 3 + GB ≧30
		≧10^5 CFU/mL 2 uropathogèns (prédominance 1 vs 2) + GB ≧30	≧10^5 CFU/mL flore mixte + GB ≧30	
		>10^4 et <10^5 CFU/mL 2 uropathogènes (ensemble) + GB ≧30		
		10^4 à <10^5 CFU/mL uropathogène (prédominance dans flore mixe) + GB≧30		

Gadalla et al. Scientific reports 2019. 10.1038/s41598-019-55523-x
Guidelines EFLM 2023 – self interpreted

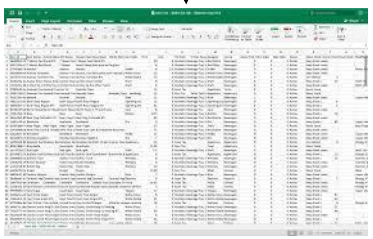
Etude SLBO

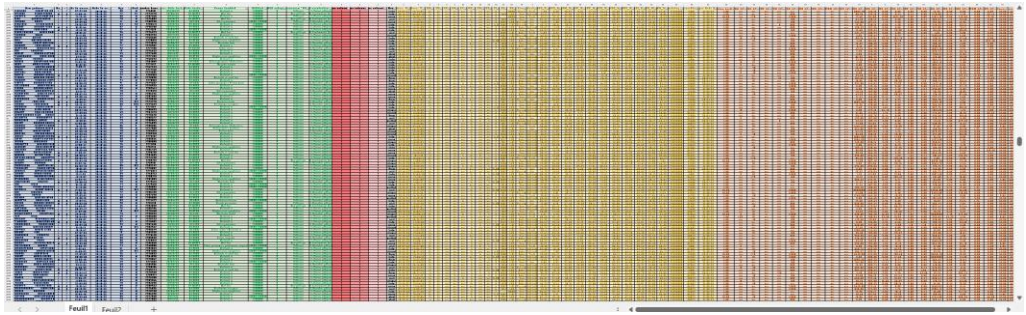
- Base de données:

Cobas 601 Cobas 701

+

LIS labo





9,753 urines
~ 400.000 données

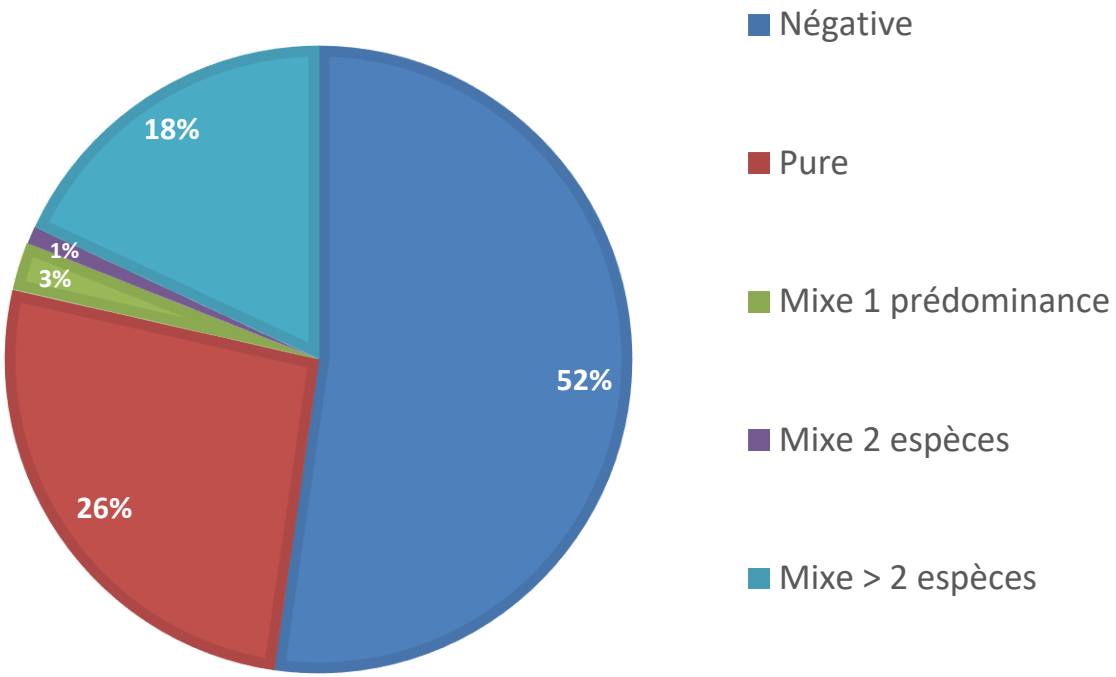
Tigette et sédiment urinaire

- **Tigette**
  - Nitrites
  - Leucocyte estérase
  - Corps cétoniques
  - Erythrocyte et hémoglobine
  - Glucose
  - Protéines
  - Bilirubine
  - Urobilinogène
  - pH
  - Densité
  - Couleur
  - Turbidité

- **Sédiment**
  - Globules blancs
  - Globules rouges
  - Cellules épithéliales
    - Squameuses
    - Non-squameuses
  - Cylindres
    - Pathologiques
    - Hyalins
  - Bactéries
  - Levures
  - Mucus
  - Cristaux

Etude SLBO

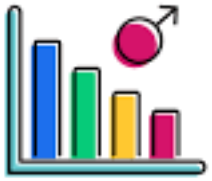
- Base de données: 9,753 urines
  - Novembre 2023 – Janvier 2024
  - Ratio femme/homme: 5,871/3,884 (60.2%/39.8%)
  - Age: moyenne = 59 ans (min-max: 0-103 ans)
    - Femmes: moyenne = 57.2 ans
    - Hommes: moyenne = 61.8 ans



NB: 1,484 *E. coli* pure (~60%)

Statistiques de base

- Approche mono ou bi-paramétrique



Mono ou bi-paramétrique

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	Test	Se/Sp (%)	VPN/VPP (%)	Accuracy (%)
EAU 2015	LEU_560	90.3/50.0	93.7/39.4	60.7
	NIT_560	41.5/95.3	82.0/76.0	81.1
	LEU_560 + NIT_560	91.8/49.7	94.4/39.6	60.8
	GB	89.3/54.4	93.4/41.3	63.6

	Test	Se/Sp (%)	VPN/VPP (%)	Accuracy (%)
PHE	LEU_560	91.6/49.4	94.8/36.9	59.7
	NIT_560	43.9/95.1	84.0/74.5	82.6
	LEU_560 + NIT_560	93.2/49.1	95.7/37.2	59.9
	GB	90.4/53.6	94.5/38.7	62.6

	Test	Se/Sp (%)	VPN/VPP (%)	Accuracy (%)
POETIC	LEU_560	95.7/49.7	97.5/35.9	60.1
	NIT_560	47.3/95.3	86.0/74.6	84.3
	LEU_560 + NIT_560	97.3/49.3	98.4/36.1	60.2
	GB	94.9/54.0	97.3/37.8	63.3

Mono ou bi-paramétrique

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	Test	Se/Sp (%)	VPN/VPP (%)	Accuracy (%)
EFLM (1)	LEU_560	99.7/50.6	99.8/36.8	61.6
	NIT_560	44.9/94.7	85.9/71.2	83.8
	LEU_560 + NIT_560	99.8/49.8	99.9/36.4	61.0
	GB	100/55.2	100/39.1	65.2

	Test	Se/Sp (%)	VPN/VPP (%)	Accuracy (%)
EFLM (2)	LEU_560	99.8/49.6	99.9/34.1	60.0
	NIT_560	46.2/93.9	87.0/66.5	84.0
	LEU_560 + NIT_560	99.8/48.8	99.9/33.8	59.4
	GB	100/54.1	100/36.3	63.6

Mono ou bi-paramétrique

BMC Urology

BioMed Central

Research article

Open Access

The urine dipstick test useful to rule out infections. A meta-analysis of the accuracy

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Conclusions: Overall, this review demonstrates that the urine dipstick test alone seems to be useful in all populations to exclude the presence of infection if the results of both nitrites and leukocyte-esterase are negative. Sensitivities of the combination of both tests vary between 68 and 88% in different patient groups, but positive test results have to be confirmed. Although the combination of positive test results is very sensitive in family practice, the usefulness of the dipstick test alone to rule in infection remains doubtful, even with high pre-test probabilities.

Mono ou bi-paramétrique

Table 2: Diagnostic performance of nitrite and leucocyte results relative to quantitative urine culture.

Culture	Sensitivity (%) (95% CI)	Specificity (%) (95% CI)	PPV (%) (95% CI)	NPV (%) (95% CI)	+LR (95% CI)	−LR (95% CI)
NIT+	27.7 (17.3–40.2)	98.4 (96.4–99.4)	75.0 (53.3–90.2)	88.4 (84.9–91.3)	16.8 (6.93–40.72)	0.74 (0.63–0.86)
LE+	60.0 (47.1–72.0)	73.9 (69.1–78.3)	29.1 (21.6–37.7)	91.2 (87.4–94.2)	2.30 (1.77–2.99)	0.54 (0.40–0.73)
NIT+ or LE+	72.3 (59.8–89.7)	72.5 (67.6–77.1)	32.0 (24.5–40.2)	93.6 (90.1–96.2)	2.63 (2.10–3.30)	0.38 (0.26–0.57)
NIT+ and LE+	16.9 (8.8–28.3)	99.7 (98.5–100)	91.7 (61.5–99.8)	87.1 (83.4–90.1)	61.6 (8.1–69.04)	0.83 (0.75–0.93)

NIT = nitrite, LE = leucocyte esterase, PPV = positive predictive value, NPV = negative predictive value, +LR = positive likelihood ratio, −LR = negative likelihood ratio.

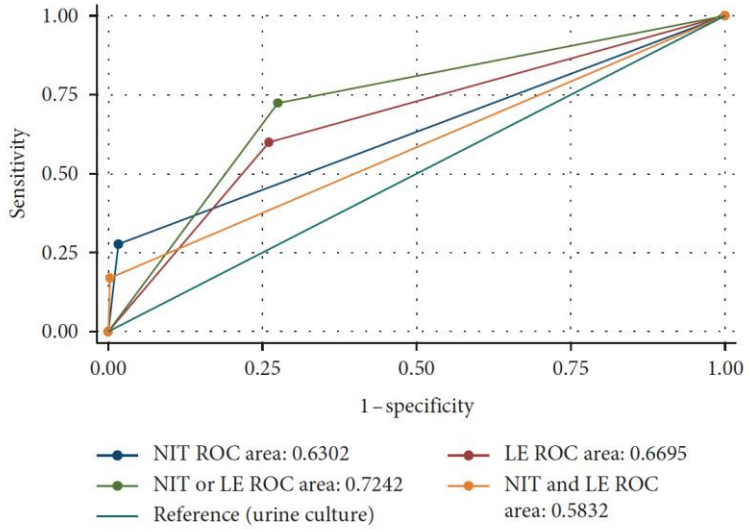

Figure 1: ROC curve for dipstick diagnosis with urine culture as a gold standard. NIT = nitrite, LE = leucocyte esterase.

Dadzie et al. 2019 Canadian Journal of Infectious Diseases and Medical Microbiology, https://doi.org/10.1155/2019/8642628

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Approche multi-paramétres

- 27 variables
  - Sédiment
  - Tigette
  - Age et sexe

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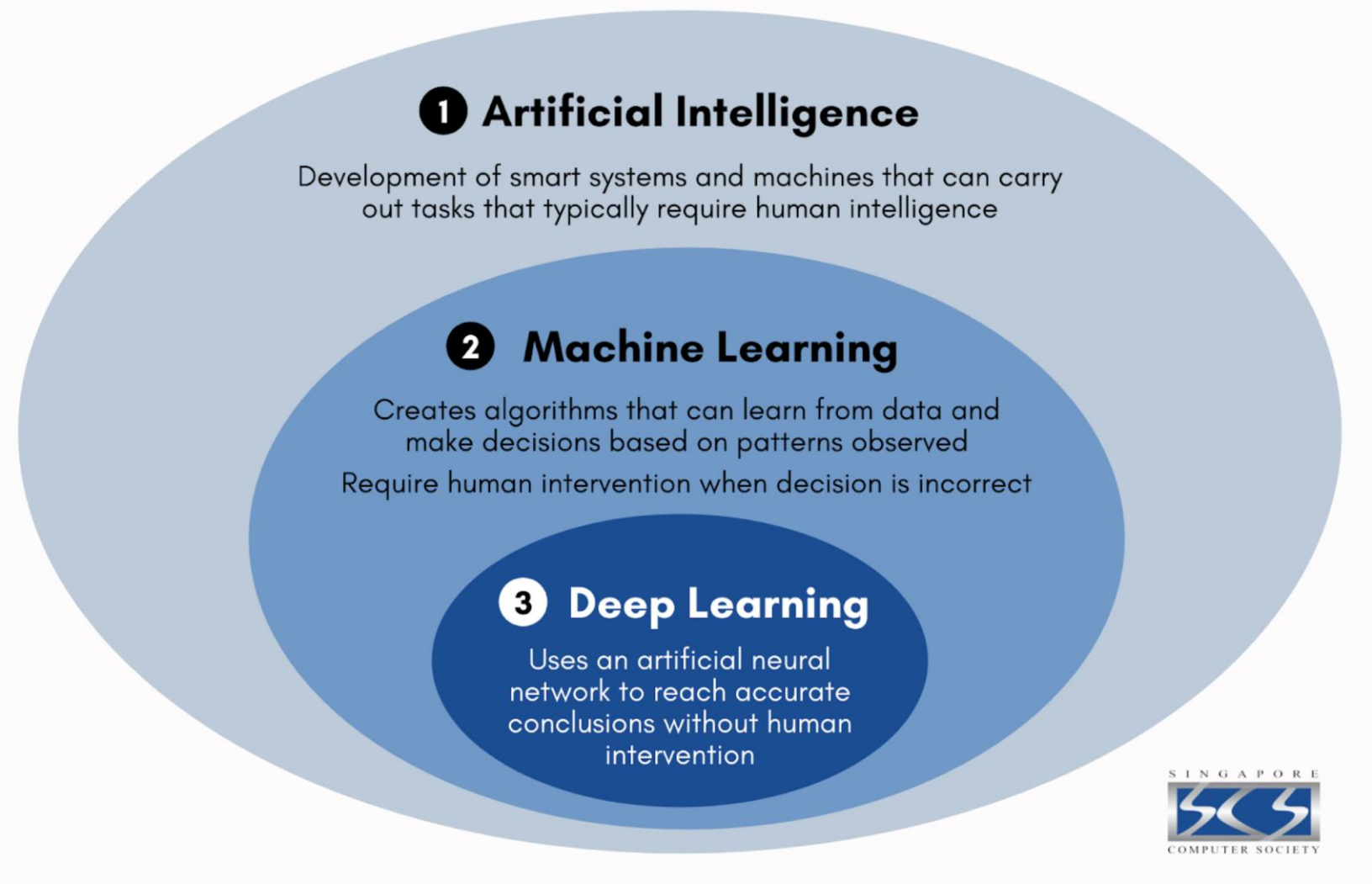

https://www.scs.org.sg/articles/machine-learning-vs-deep-learning, consulté le 22/03/2024, 16h48

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- Notions de « Machine learning »

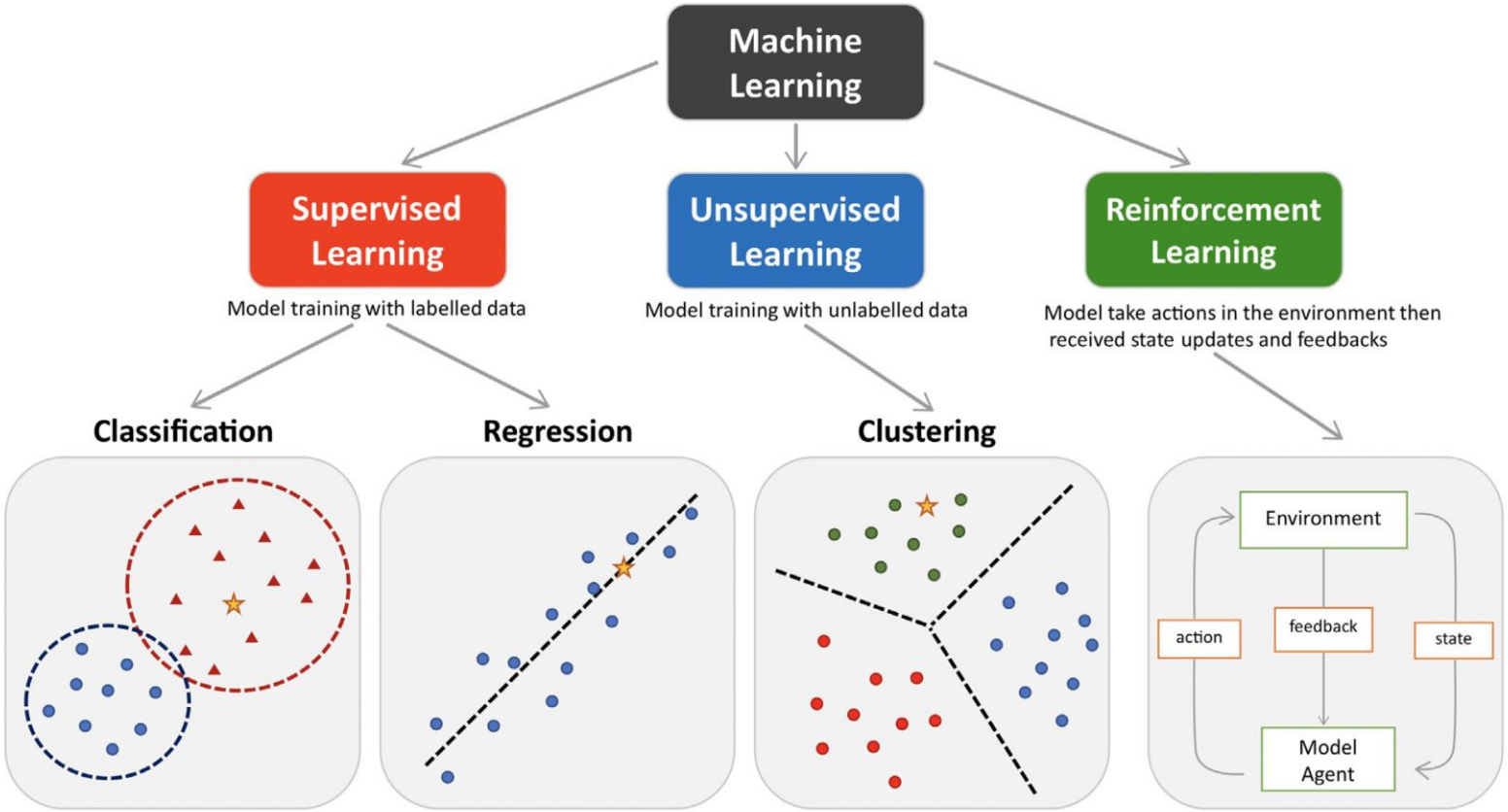

FIGURE 1 | The main types of machine learning. Main approaches include classification and regression under the supervised learning and clustering under the unsupervised learning. Reinforcement learning enhance the model performance by interacting with environment. Coloured dots and triangles represent the training data. Yellow stars represent the new data which can be predicted by the trained model.

Peng et al. Front Pharmacology (2021) 10.3389/fphar.2021.720694

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- Notions de « Machine learning »

1. Obtention d'un modèle

A. Base de données pour l'apprentissage (**6,827 urines**)

B. Obtention d'un modèle

C. Evaluation des performances

2. Validation du modèle

A. Base de données pour la validation (**2,926 urines**)

B. Vérification des performances à partir du modèle

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- Etude SLBO: modèles utilisés:

- Multiple Logistic Regression
- Support Vector Machine (SVM)
- Random Forest
- XGBoost
- CatBoost
- Multilayer Perceptron (MLP)

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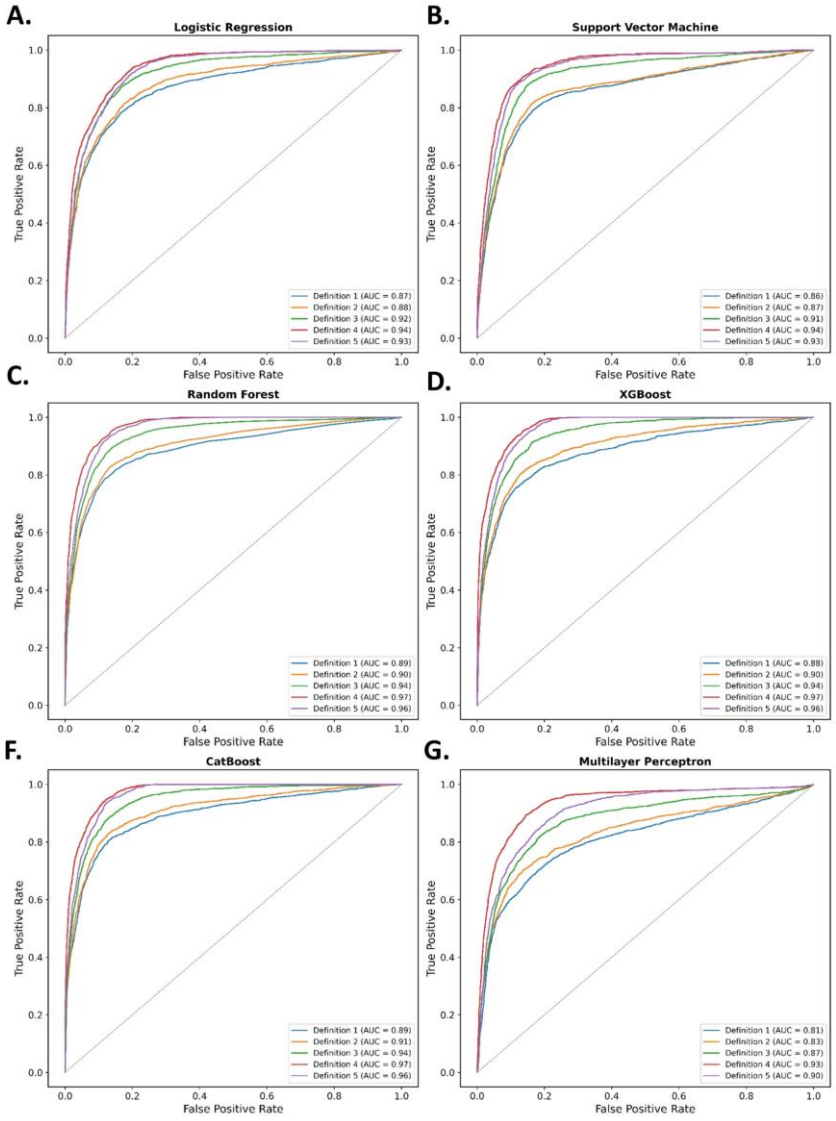
Logistic regression
Définition 1: 0.87
Définition 2: 0.88
Définition 3: 0.92
Définition 4: 0.94
Définition 5: 0.93

Random forrest
Définition 1: 0.89
Définition 2: 0.90
Définition 3: 0.94
Définition 4: 0.97
Définition 5: 0.96

CatBoost
Définition 1: 0.89
Définition 2: 0.91
Définition 3: 0.94
Définition 4: 0.97
Définition 5: 0.96



Support Vector Machine
Définition 1: 0.86
Définition 2: 0.87
Définition 3: 0.91
Définition 4: 0.94
Définition 5: 0.93

XGBoost
Définition 1: 0.88
Définition 2: 0.90
Définition 3: 0.94
Définition 4: 0.97
Définition 5: 0.96

Multilayer Perceptron
Définition 1: 0.81
Définition 2: 0.83
Définition 3: 0.87
Définition 4: 0.93
Définition 5: 0.90

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Table 1. Performance metrics of the CatBoost classifiers for the 7-fold stratified cross-validation procedure and predictions on the test set.

Model	Optimal threshold	Dataset	Sensitivity (%, CI)	Specificity (%, CI)	PPV (%, CI)	NPV (%, CI)	Accuracy (%, CI)	AUC (%, CI)
Definition 1	0.2575	Validation	82.2 (77.4-86.4)	86.5 (81.5-89.5)	68.8 (61.4-73.0)	93.1 (91.7-94.6)	85.3 (81.7-87.4)	89.5 (87.5-91.4)
		Test	77.9 (74.9-80.7)	86.8 (85.3-88.2)	68.0 (65.0-70.9)	91.6 (90.4-92.7)	84.4 (83.2-85.7)	88.2 (86.7-89.7)
Definition 2	0.2422	Validation	84.7 (81.5-90.0)	86.8 (84.5-90.4)	67.6 (64.2-73.8)	94.6 (93.5-96.4)	86.3 (84.4-88.8)	91.3 (89.9-92.7)
		Test	79.3 (76.3-82.1)	88.0 (86.7-89.3)	68.1 (65.2-71.2)	93.0 (91.8-94.0)	85.9 (84.7-87.1)	90.0 (88.5-91.3)
Definition 3	0.2318	Validation	90.2 (87.4-93.7)	87.3 (84.5-91.1)	67.9 (63.2-74.3)	96.8 (96.0-97.9)	88.0 (85.8-90.3)	94.5 (93.5-95.2)
		Test	87.9 (85.3-90.3)	87.8 (86.4-89.1)	67.9 (64.9-71.0)	96.1 (95.2-96.9)	87.8 (86.6-89.0)	94.7 (93.8-95.5)
Definition 4	0.2459	Validation	94.9 (92.7-95.9)	88.9 (87.7-90.1)	71.2 (69.2-73.0)	98.4 (97.7-98.7)	90.3 (89.5-91.1)	97.3 (96.7-97.7)
		Test	90.5 (88.4-92.6)	90.7 (89.5-91.8)	73.7 (70.7-76.7)	97.1 (96.4-97.7)	90.7 (89.6-91.7)	97.2 (96.7-97.6)
Definition 5	0.2333	Validation	94.5 (90.1-98.0)	87.4 (83.6-90.8)	66.5 (60.6-72.6)	98.4 (97.1-99.4)	88.9 (86.3-91.3)	96.3 (95.2-97.0)
		Test	91.7 (89.4-93.9)	90.0 (88.8-91.2)	70.6 (67.5-73.6)	97.7 (97.0-98.2)	90.4 (89.3-91.4)	96.8 (96.2-97.3)

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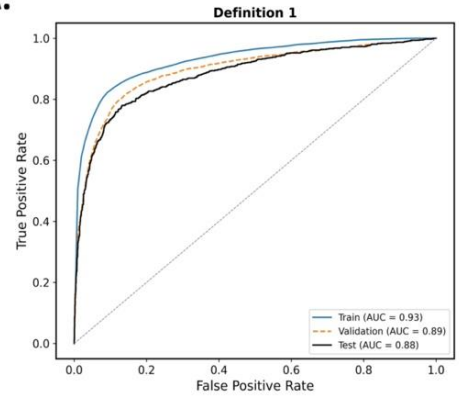
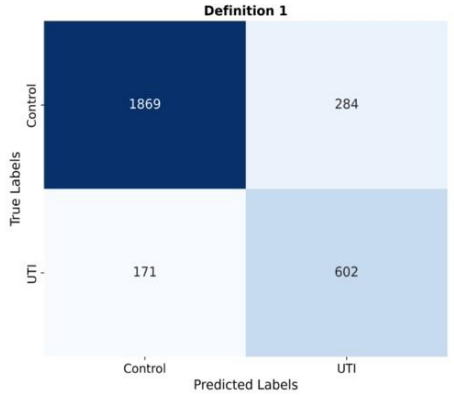
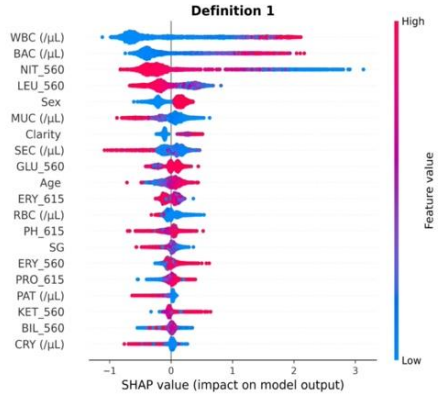
A.







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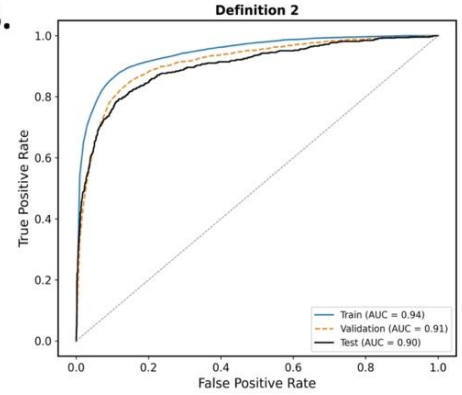

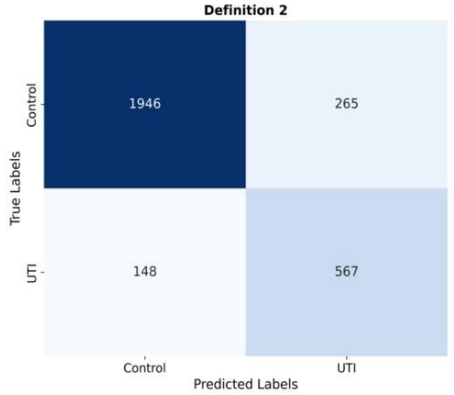

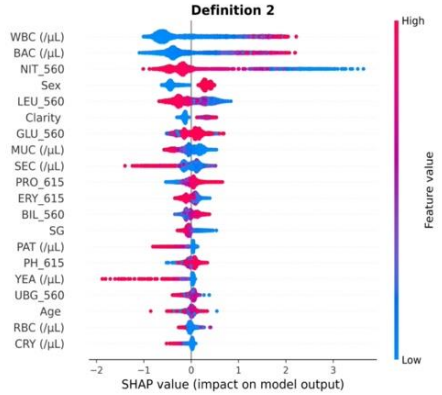

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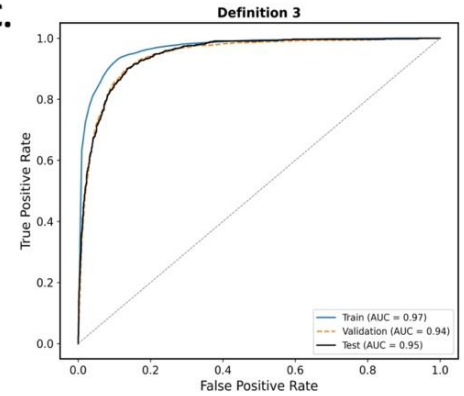
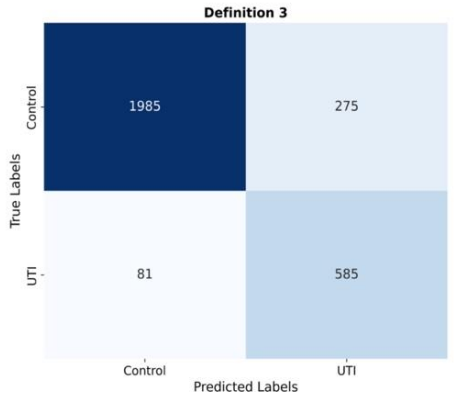
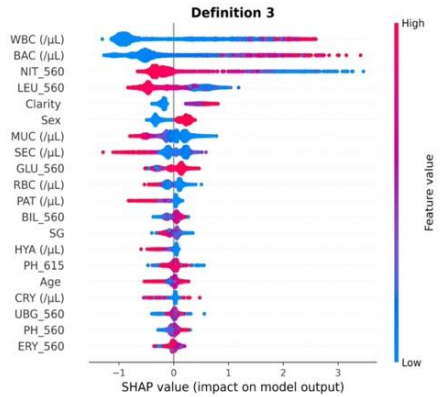
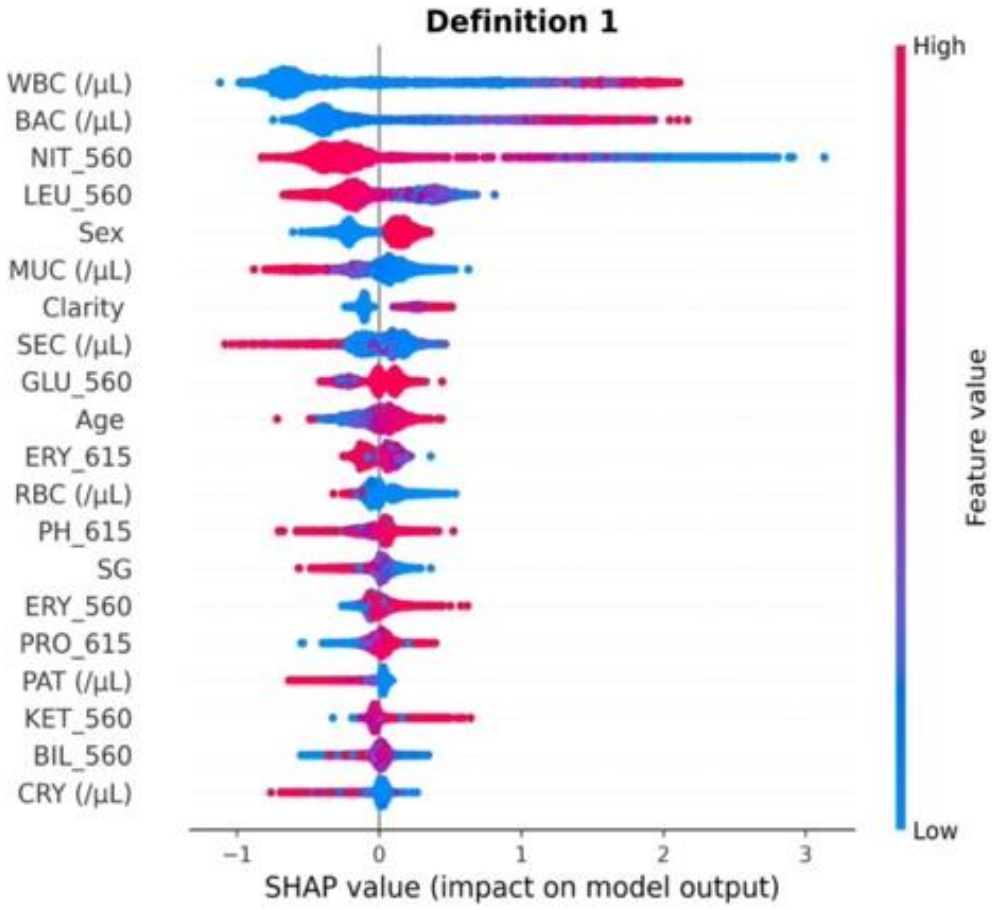




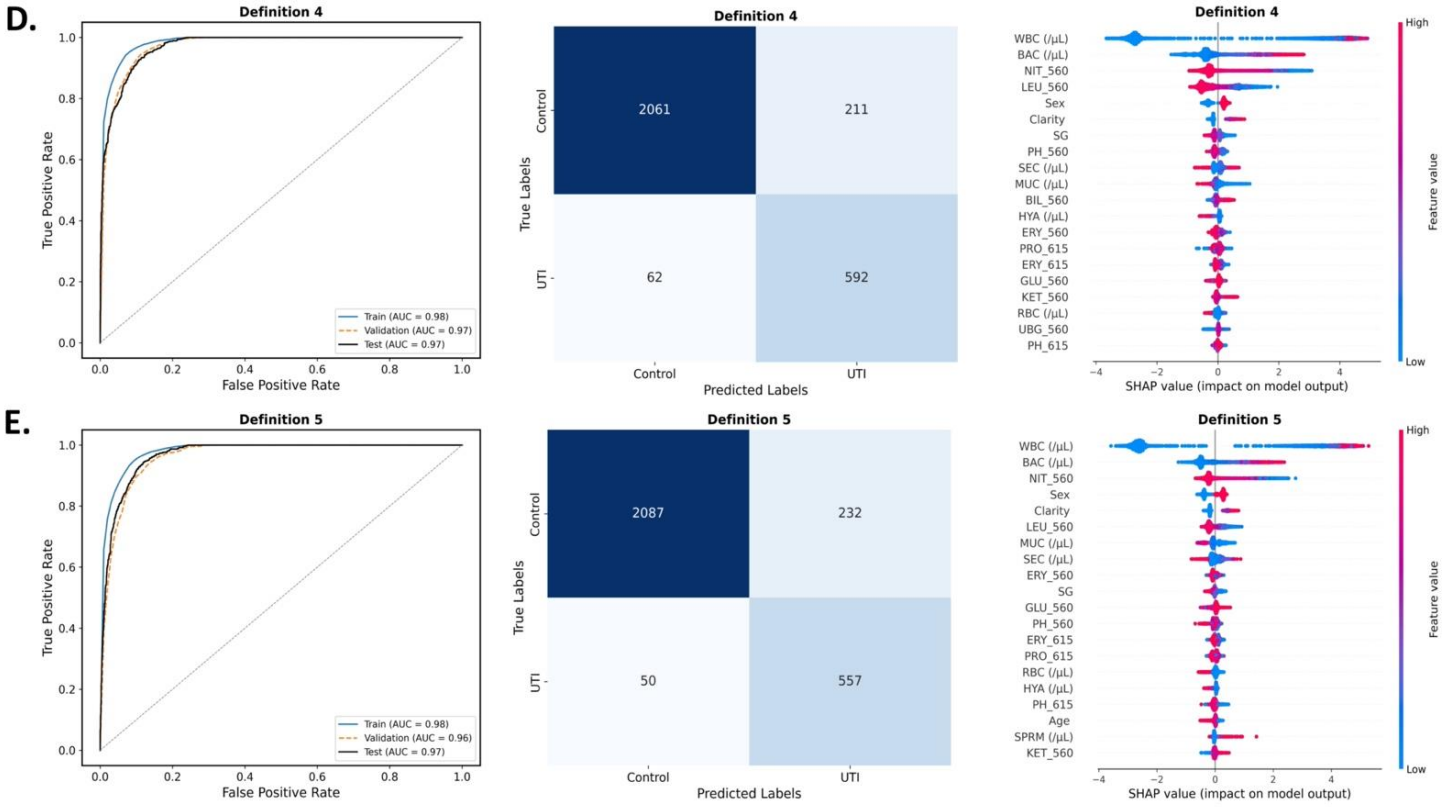


Intelligence artificielle



- **Beeswarm plot:**
  - SHAP = SHapley Additive exPlanations
  - Contribution de chaque variable dans le modèle
  - Impact élevé = en haut
  - Bleu = valeur élevée
  - Rouge = valeur faible

Intelligence artificielle



Statistiques simples versus avancées

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Accuracy (%)	Définition 1	Définition 2	Définition 3	Définition 4	Définition 5
LEU_560	60.7	59.7	60.1	61.6	60.0
NIT_560	81.1	82.6	84.3	83.8	84.0
LEU_560 + NIT_560	60.8	59.9	60.2	61.0	59.4
GB	63.6	62.6	63.3	65.2	63.6
ML (validation)*	85.3	86.3	88.0	90.3	88.9
ML (test)*	84.4	85.9	87.8	90.7	90.4

*CatBoost model

Accuracy (%)	Couleur
50-60	
60-70	
70-80	
80-90	
90-100	

Intelligence artificielle

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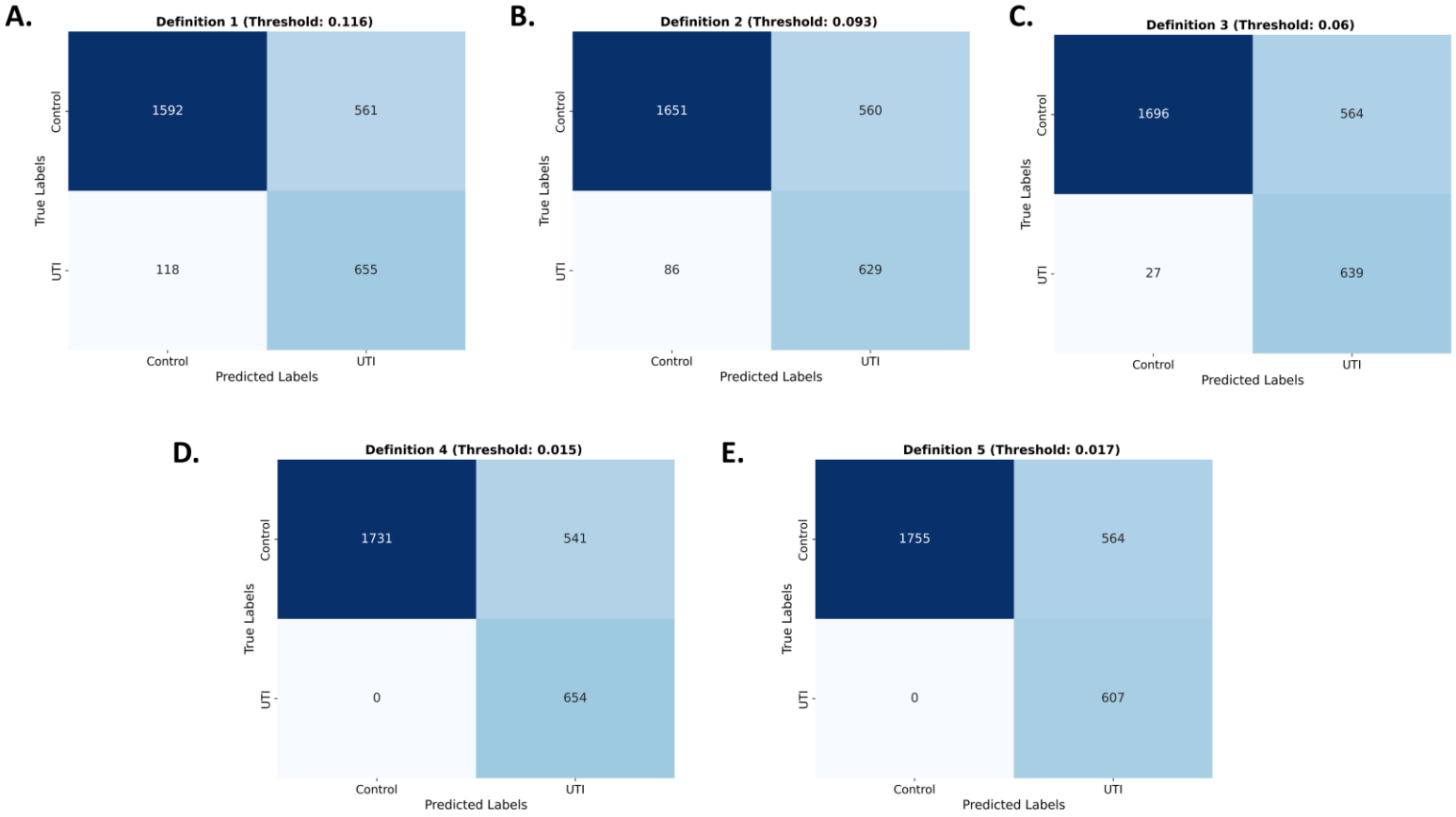

Intelligence artificielle

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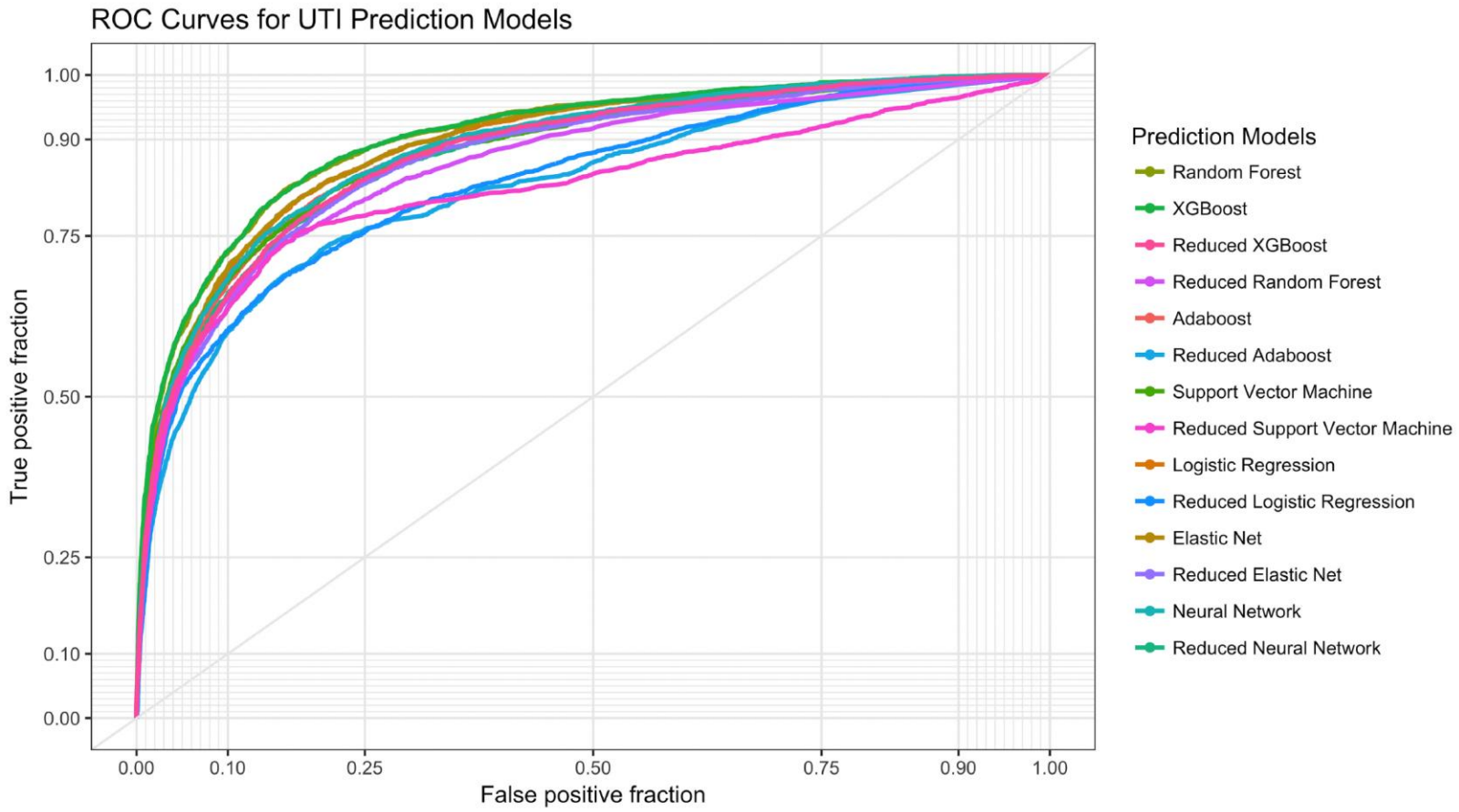
Model	Sensitivity-tuned threshold	Sensitivity (%, CI)	Specificity (%, CI)	PPV (%, CI)	NPV (%, CI)	Accuracy (%, CI)
Definition 1	0.116	84.6 (82.1-87.0)	74.0 (72.1-75.6)	53.9 (51.0-56.5)	93.1 (91.9-94.2)	76.8 (75.3-78.2)
Definition 2	0.093	88.0 (85.5-90.3)	74.6 (72.8-76.5)	53.0 (50.0-55.9)	95.0 (94.0-95.6)	77.9 (76.4-79.3)
Definition 3	0.06	95.6 (94.4-97.4)	75.1 (73.2-76.8)	53.2 (50.5-55.8)	98.4 (97.8-99.0)	79.8 (78.4-81.2)
Definition 4	0.015	100 (100-100)	76.2 (74.4-78.0)	54.7 (52.0-57.5)	100 (100-100)	81.5 (80.1-82.9)
Definition 5	0.017	100 (100-100)	75.7 (73.8-77.5)	51.8 (48.8-54.7)	100 (100-100)	80.7 (79.2-82.1)

Intelligence artificielle - discussion



- 212 versus 10 variables
- <u>Outcome:</u> >10^4 CFU/HPF (2) flore mixte si *E. coli* présent
- Modèle comparé au jugement clinique (AB pour IU ou catégorisation IU)

Taylor et al. Plos One (2018) 10.1371/journal.pone.0194085

Intelligence artificielle - discussion

Clinique Saint-Luc Bouge

Table 4. Test characteristics of UTI prediction models on validation data*.

Models	AUC (95%CI)	Sensitivity (95% CI)	Specificity (95% CI)	+LR (95% CI)	-LR (95% CI)	Accuracy (95% CI)	P–value
XGBoost	**.904(.898-.910)**	61.7(60.0–63.3)	94.9 (94.5–95.3)	12.0(11.1–13.0)	.404(.387-.421)	87.5 (87.0–88.0)	NA
Random Forest	.902(.896-.908)	57.3(55.6–58.9)	96.0 (95.6–96.3)	14.3(13.0–15.6)	.445(.428-.462)	87.4 (86.9–87.9)	0.58
Adaboost	.880(.874-.887)	62.2(60.6–63.8)	92.3(91.8–92.7)	8.06(7.54–8.61)	.409(.392-.427)	85.6(85.1–86.2)	< .001
Support Vector Machine	.878(.871-.884)	49.6(47.9–51.2)	96.8(96.4–97.1)	15.3(13.8–16.9)	.521(.504-.538)	86.3(85.7–86.8)	< .001
ElasticNet	.892(.885-.898)	56.8(55.2–58.4)	94.9(94.5–95.2)	11.1(10.2–12.0)	.455(.438-.473)	86.4(85.9–87.0)	< .001
Logistic Regression	.891 (.884-.897)	57.5(55.8–59.1)	94.7(94.3–95.1)	10.9(10.0–11.8)	.449(.432-.466)	86.4(85.9–87.0)	< .001
Neural Network	.884 (.878-.890)	54.6(52.9–56.2)	95.3(95.0–95.7)	11.7(10.8–12.8)	.476(.460-.494)	86.3(85.8–86.8)	<001
Reduced XGBoost	**.877(.871-.884)**	54.7(53.0–56.3)	94.7(94.3–95.1)	10.4(9.6–11.3)	.479(.462-.496)	85.9(85.3–86.4)	< .001
Reduced Random Forest	.861(.853-.868)	54.8(53.1–56.4)	94.3(93.9–94.7)	9.66(8.94–10.4)	.479(.462-.497)	85.5(85.0–86.1)	< .001
Reduced Adaboost	.826(.817-.834)	61.9(60.3–63.5)	88.8(88.2–89.3)	5.50(5.21–5.81)	.429(.412-.448)	82.8(82.2–83.3)	< .001
Reduced Support Vector Machine	.822(.813-.832)	49.4(47.8–51.1)	95.8(95.4–96.1)	11.7(10.7–12.9)	.528(.511-.546)	85.5(84.9–86.0)	< .001
Reduced Elastic Net	.870(.863-.877)	52.4(50.7–54.1)	95.2(94.8–95.5)	10.9(9.99–11.8)	.500(.482-.571)	85.7(85.1–86.2)	< .001
ReducedLogistic Regression	.870(.863-.877)	53.3(51.6–54.9)	94.8(94.4–95.2)	10.3(9.52–11.2)	.492(.476-.510)	85.6(85.0–86.2)	< .001
Reduced Neural Network	.873(.867-.881)	54.0(52.3–55.6)	95.0(94.6–95.4)	10.9(10.0–11.8)	.485(.468-.502)	85.9(85.4–86.5)	< .001

- XGBoost = meilleur modèle (full and reduced, $p > 0.05$)
- Modèle ML versus jugement clinique
  - FP ↓ 29.6-33.3%
  - FN ↓ 33.2-38.7%

Table 2. Selected variables for reduced models.

Variable	References
Age	[3, 21]
Gender	[3, 6, 21]
UA Leukocytes	[3, 6, 10, 12, 21]
UA Nitrites	[3, 6, 10, 12, 21]
UA WBC	[3, 6, 10, 12, 21]
UA Bacteria	[3, 6, 10, 12, 21]
UA Blood	[3, 6, 10, 12, 21]
UA Epithelial Cells	[3, 6, 10, 12, 21]
History of UTI	[3, 6, 21]
Dysuria	[3, 6, 21]

Taylor et al. Plos One (2018) 10.1371/journal.pone.0194085

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Table 2 Feature selection by recursive feature elimination using a Random Forest Classifier. Feature importance is shown as well as the individual AUC score

	RFE Ranking	RF Feature Importance	Individual AUC[a]
WBC count	1	0·30	0·82
Bacterial count	1	0·30	0·71
Age	1	0·12	0·63
Epithelial cell count	1	0·07	0·49
RBC count	1	0·06	0·56
# of positive cultures to date	1	0·03	0·60
Pyuria, no RBCs	1	0·02	0·57
Pregnant	1	0·02	0·57
Inpatient	1	0·01	0·53
Gender	1	0·01	0·53
Persistent/recurrent infection	1	0·01	0·55
# of positive cultures month prior	1	0·009	0·53
Positive for nitrates	1	0·008	0·52
Renal inpatient/outpatient	1	0·005	0·50
Pre-operative patient	1	0·004	0·51
Acute kidney disease	1	0·003	0·50
Immunocompromised	2	0·002	0·50
# of positive cultures week prior	3	0·002	0·51
Multiple Sclerosis	4	0·001	0·50
Offensive smell	5	0·0007	0·50
Haematuria, no WBCs	6	0·0001	0·50

[a]Individual AUC score is calculated from a Logistic Regression classifier, where the feature in question is the sole independent variable

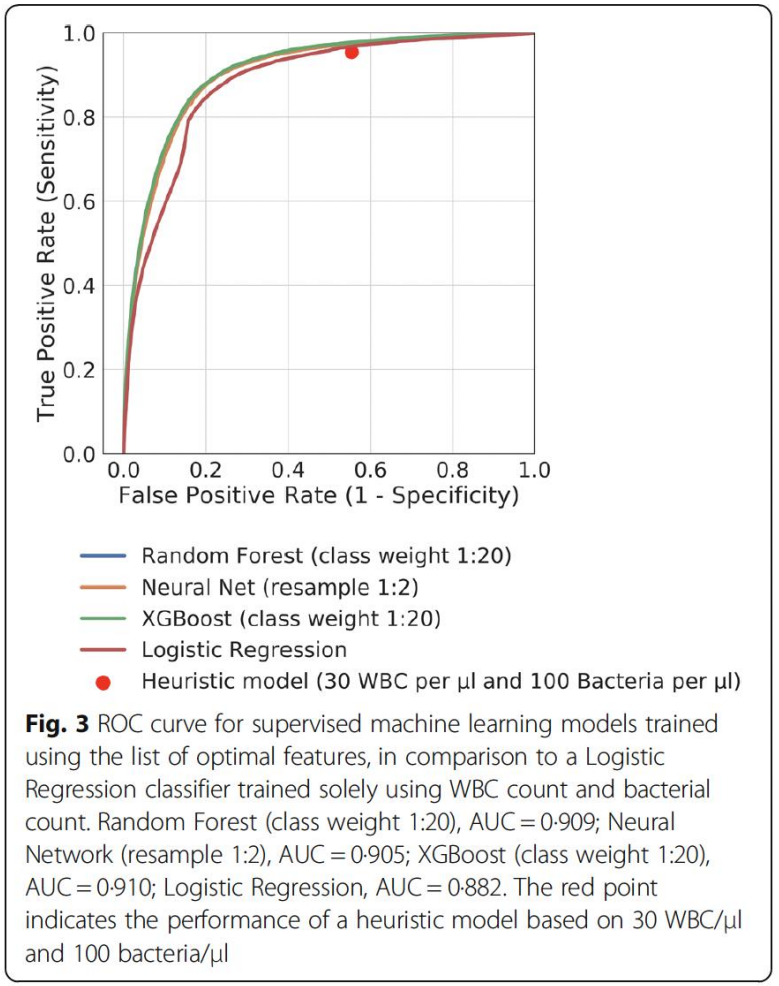

Fig. 3 ROC curve for supervised machine learning models trained using the list of optimal features, in comparison to a Logistic Regression classifier trained solely using WBC count and bacterial count. Random Forest (class weight 1:20), AUC = 0·909; Neural Network (resample 1:2), AUC = 0·905; XGBoost (class weight 1:20), AUC = 0·910; Logistic Regression, AUC = 0·882. The red point indicates the performance of a heuristic model based on 30 WBC/µl and 100 bacteria/µl

Burton et al. BMC Medical Informatics and Decision Making (2019), https://doi.org/10.1186/s12911-019-0878-9

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Table 3 Comparison of performance for heuristic and machine learning models tested on holdout data

Model Name	AUC Score	Accuracy (%)	*p*-value**	PPV	NPV	Sensitivity (%)			Specificity (%)	Relative Workload Reduction (%)
						All Patients	Pregnant	Children < 11 Yrs		
Heuristic model (30 WBC/μl or 100 bacteria/μl)		63·92	NA	42.73 [± 0.51]	97.01 [±0.28]	95·70 [± 0·15]	85·9 [± 0·72]	91·5 [± 0·92]	52·10 [± 0·36]	39·06 [± 0·38]
Random Forest (Class weight - 1:20)	0·908	71·96	< 0.001	40.47 [± 0.54]	97.67 [± 0.25]	95·95 [± 0·23]	70·5 [± 2·14]	89·8 [± 1·49]	63·40 [± 0·54]	47·58 [± 0·39]
Neural Network	0·906	85·00	< 0.001	71.70 [± 0.46]	90.18 [± 0.50]	74·03 [± 0·64]	27·6 [± 5·74]	69·3 [± 3·38]	89·09 [± 0·29]	71·98 [± 0·35]
Neural Network (with resampling*)	0·904	79·35	< 0.001	57.66 [± 0.74]	95.54 [± 0.19]	90·60 [± 0·35]	56·6 [± 3·43]	84·8 [± 2·04]	75·16 [± 0·44]	57·33 [± 0·38]
XGBoost (Class weight - 1:20)	0·910	65·68	< 0.001	44.05 [± 0.74]	97.77 [± 0.13]	96·70 [± 0·18]	77·1 [± 1·65]	93·1 [± 1·13]	54·14 [± 0·61]	40·36 [± 0·38]

[95% Confidence Interval]
*Resampling (without replacement) at a ratio of 2:1 for positive samples to offset class imbalance
** *p*-values obtained by comparison to heuristic model by McNemar test

Burton et al. BMC Medical Informatics and Decision Making (2019), https://doi.org/10.1186/s12911-019-0878-9

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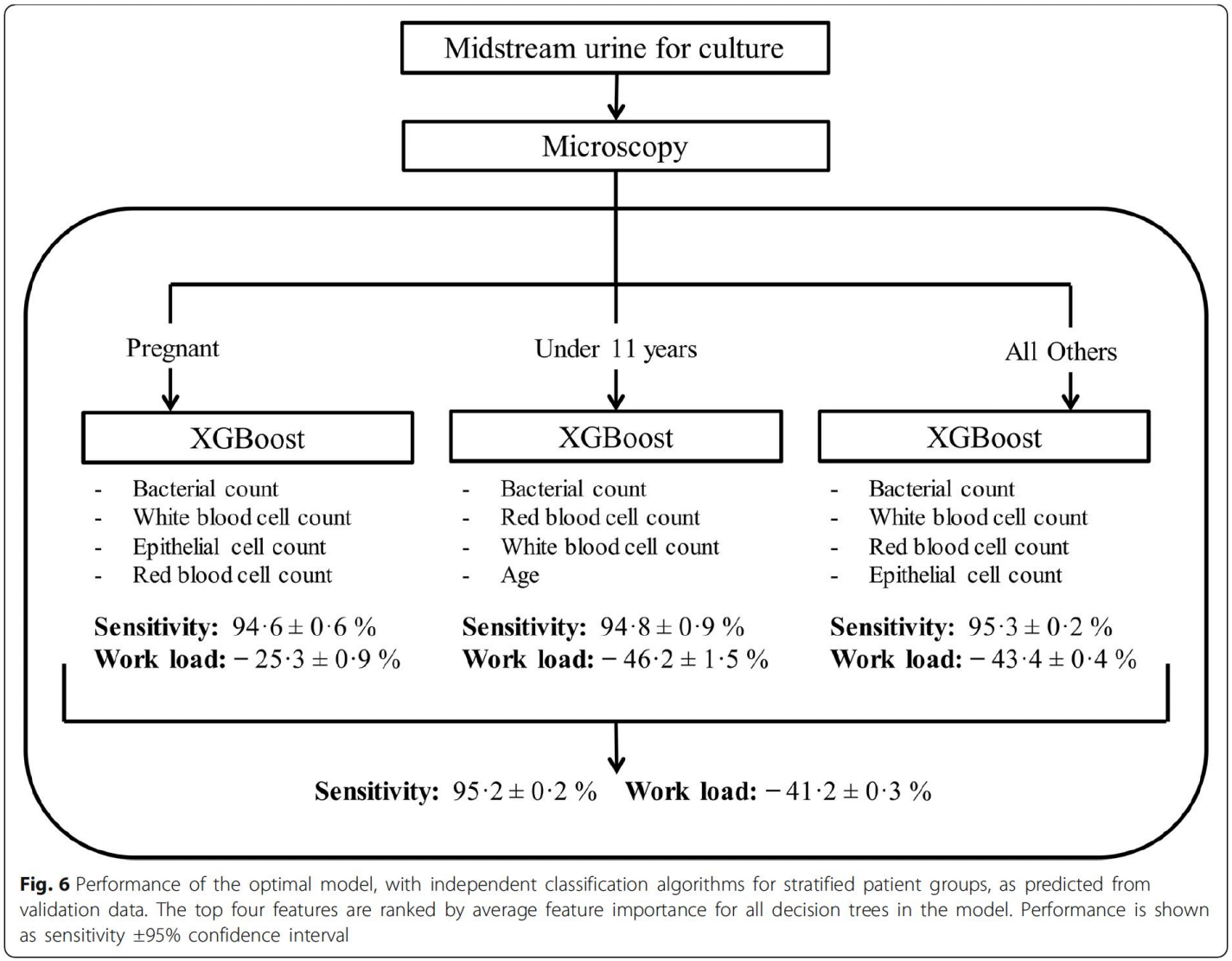
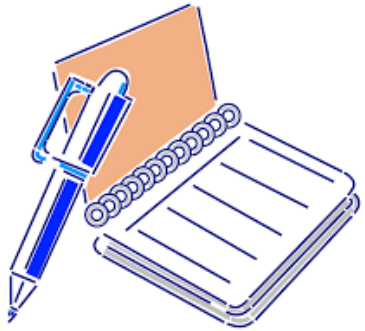


Fig. 6 Performance of the optimal model, with independent classification algorithms for stratified patient groups, as predicted from validation data. The top four features are ranked by average feature importance for all decision trees in the model. Performance is shown as sensitivity ±95% confidence interval

Burton et al. BMC Medical Informatics and Decision Making (2019), https://doi.org/10.1186/s12911-019-0878-9

Intelligence artificielle

- Remarques:
  - Pas d'inclusion des symptômes cliniques
    - *« The diagnosis of UTI by clinical criteria alone has an error rate of approximately **33%*** »*
    - *Variabilité inter-individuelle/subjectivité*
  - Prise d'antibiotiques? Problèmes pré-analytique?
    - *Etude « real-life » sans exclusion de 0 à 104 ans*
  - Trop dur à implémenter en routine?
    - Modèles compliqués. Logiciel/Middleware/application
    - Utiliser un modèle plus simple dans un LIS?



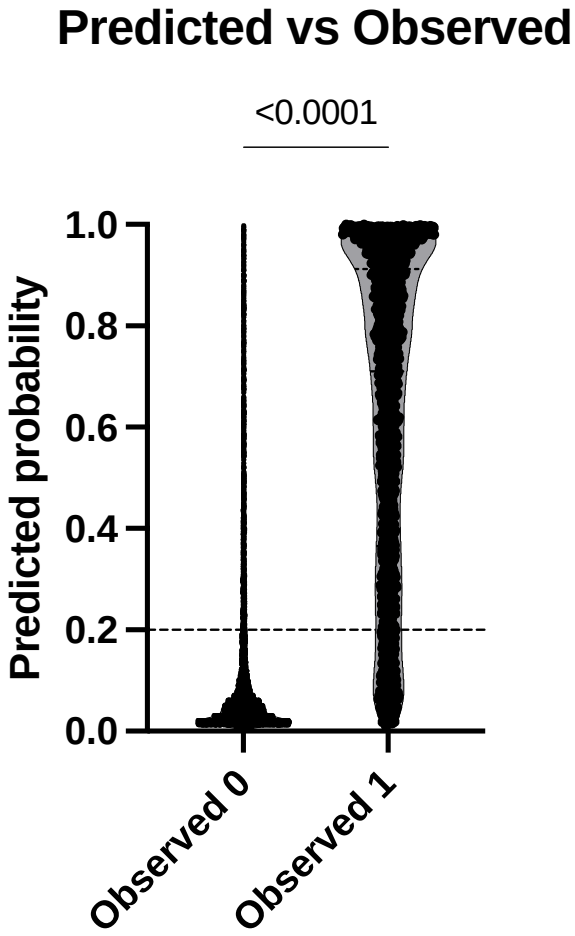
*Schmiemann et al. 2010 Dtsch Arztebl Int; 107(21): 361–7

Intelligence artificielle

- GraphPad Prism Mac 10.2.0 (335)
  - Equation

$$\hat{p} = \frac{\exp(b_0 + b_1X_1 + b_2X_2 + \ldots + b_pX_p)}{1 + \exp(b_0 + b_1X_1 + b_2X_2 + \ldots + b_pX_p)}$$

  - Calcul d'une probabilité de **0 à 1** pour chaque échantillon
  - Probabilité comparée à l'outcome **0 ou 1**



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- GraphPad Prism Mac 10.2.0 (335)

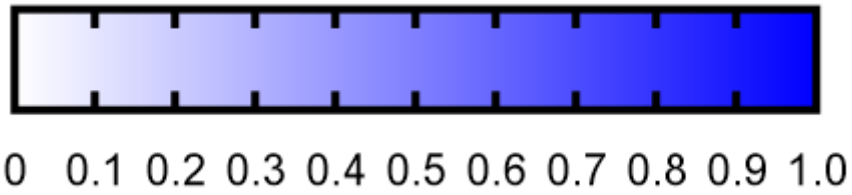
Area under the ROC curve				
Area	**0,9284**			
Std. Error	0,003044			
95% confidence interval	0,9225 to 0,9344			
P value	<0,0001			
Classification table	Predicted 0	Predicted 1	Total	% Correctly classified
Observed 0	6474	1060	7534	85,93
Observed 1	311	1908	2219	85,98
Total	6785	2968	9753	85,94
Negative predictive power (%)	**95,42**			
Positive predictive power (%)	**64,29**			
Classification cutoff	0,2			

Retour aux cas cliniques…

	Cas #1	**Cas #2**
Tigette/sédiment	- Femme - 37 ans - NIT + - LEU +++ - GB 172/µL	- Femme - 41 ans - NIT + - LEU +++ - GB 160/µL
Microbiologie	**Culture négative**	***E. coli* CFU >10^5/mL**
Prédiction machine learning (0 à 1)	**Score 0.003 ➔ négatif**	**Score 0.961 ➔ positif**

Conclusion et perspective

- **Intelligence artificielle comme aide au diagnostic**
  - Possibilité d'exclure rapidement une infection urinaire sur base d'un score de prédiction



0-0.2: Très peu probable
0.2-0.5: Peu probable
0.5-0.8: Probable
0.8-1.0: Très probable

  - Besoin d'une définition harmonisée
  - Besoin d'une validation externe
  - Evaluation prospective du réel apport (AB)