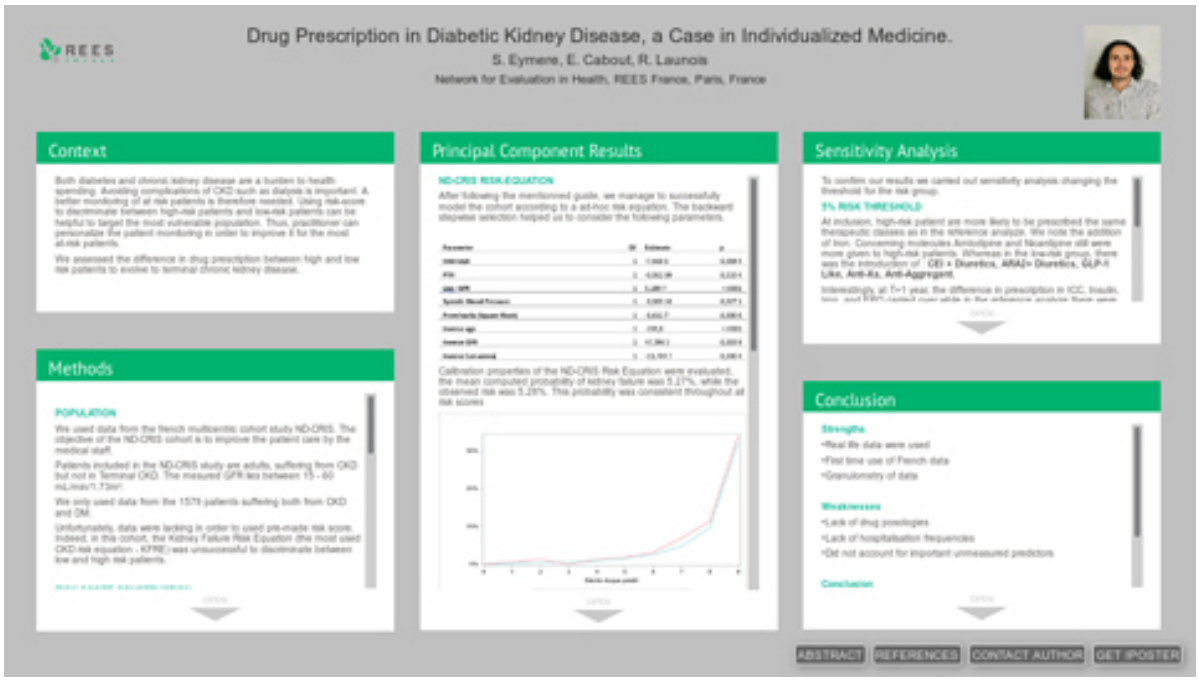
# Drug Prescription in Diabetic Kidney Disease, a Case in Individualized Medicine.

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**PRESENTED AT:**

# CONTEXT

Both diabetes and chronic kidney disease are a burden to health spending. Avoiding complications of CKD such as dialysis is important. A better monitoring of at risk patients is therefore needed. Using risk-score to discriminate between high-risk patients and low-risk patients can be helpful to target the most vulnerable population. Thus, practitioner can personalize the patient monitoring in order to improve it for the most at-risk patients.

We assessed the difference in drug prescription between high and low risk patients to evolve to terminal chronic kidney disease.

# METHODS

**POPULATION**

We used data from the french multicentric cohort study ND-CRIS. The objective of the ND-CRIS cohort is to improve the patient care by the medical staff.

Patients included in the ND-CRIS study are adults, suffering from CKD but not in Terminal CKD. The mesured GFR lies between 15 - 60 mL/min/1.73m².

We only used data from the 1579 patients suffering both from CKD and DM.

Unfortunately, data were lacking in order to used pre-made risk score. Indeed, in this cohort, the Kidney Failure Risk Equation (the most used CKD risk equation - KFRE) was unsuccessful to discriminate between low and high risk patients.

**RISK-SCORE CONSTRUCTION**

Following the 4-part guide from Moons, Roystone and Altman, we constructed an ad-hoc risk score :

1.We imputed missing data using multiple imputation

2.We choose a logistic model to assess the probability of a patient worsening from CKD to terminal CKD.

3.We used a backward steptwise selection to include different predictors.

4.We assessed validity : we computed sensitivity and specificity of the risk-score, as well as the calibration and discrimination properties of the model. Internal validity was assessed as well.

**RISK STRATIFICATION**

We had to select a threshold. Arbitrarly we selected the 10% risk threshold. In sensitivity analysis we used 5% and 20% risk threshold. We also stratified the population in deciles according to their computed risk-score

**DRUG CONSUMPTION**

In the patient data files, drug consumption was registered. We used ATC classification to assess qualitatively patient’s drug consumption.

We use Khi-Square test to assess whether there is a significatively difference ($p<0.05$) in qualitative drug consumption between low-risk and high-risk group, at inclusion, T+1year and T+2 years.

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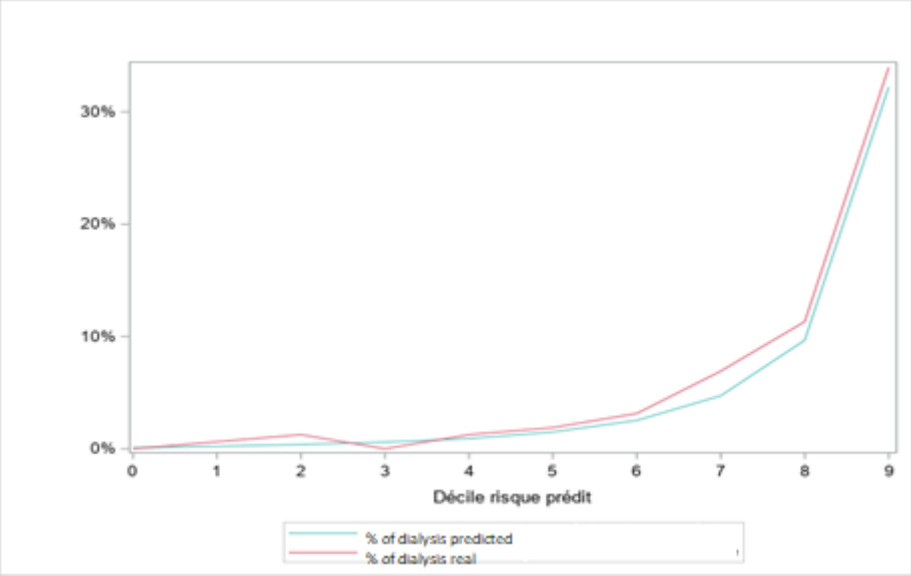
# PRINCIPAL COMPONENT RESULTS

## ND-CRIS RISK-EQUATION

After following the mentionned guide, we manage to successfully model the cohort according to a ad-hoc risk equation. The backward stepwise selection helped us to consider the following parameters.

| Parameter | DF | Estimate | p |
|---|---|---|---|
| Intercept | 1 | -7,668 6 | 0,069 4 |
| PTH | 1 | -0,002 09 | 0,010 4 |
| Log : GFR | 1 | 5,289 7 | <.0001 |
| Systolic Blood Pressure | 1 | -0,000 16 | 0,027 1 |
| Proteinuria (Square Root) | 1 | -0,612 7 | 0,000 6 |
| Inverse age | 1 | -233,8 | <.0001 |
| Inverse GFR | 1 | 47,396 5 | 0,003 9 |
| Inverse Calcaemia | 1 | -13,784 7 | 0,000 4 |

Calibration properties of the ND-CRIS Risk Equation were evaluated, the mean computed probability of kidney failure was 5.27%, while the observed risk was 5.28%. This probability was consistent throughout all risk scores




We then assessed the ND-CRIS discrimination capacity and compared it to the KFRE. At a 10% threshold we observed :

•Sensitivity : 65% (KFRE : 77% )

•Specificity : 89% (KFRE : 75% )

•Positive Predictive Value : 28% (KFRE : 17% )

•Negative Predictive Value : 98% (KFRE : 98 %)

•C-Statistic : 0.902 (KFRE : 0.83)

| Dialysis Number by Risk | | | |
|---|---|---|---|
| NDCRIS | Dialysis | | |
| | Dialysis | No dialysis | Total |
| Low risk | 33 | 1333 | 1366 |
| High risk | 63 | 160 | 223 |
| Total | 96 | 1493 | 1589 |

**DRUG CONSUMPTION DIFFERENCE AT A 10% THRESHOLD**

**At Inclusion**

At inclusion, high-risk patient are more likely to have a prescription of Anti-acid compared to low-risk patient. Other therapeutics classes includes : **Calcic Canal Inhibitors , Insulins, Iron, EPO, PTH inhibitors**.

While low risk patients are more frequently taking : **sulfamids** and **Vitamin K** antagonist to sooth the effects of the diseases.

Regarding specific molecules, Amlodipin and Nicardipin are more frequently prescribed for high-risk patients, whether metformin, gliclazide and sitgliptin are more used in low-risk patients.

**At T+1 year**

After 1 year, **CCI**, **Insulins** and **Amlodipine** are still more prescribed in high-risk patients, as well as **sulfamids** and **metformine** for low-risk patient. Notably, **ARA2** + diuretics are more prescribe at 1 year for low risk patients.

**At T+2 years**

After 2 years, **Amlodipine** is still more prescribed in high risk patients

# SENSITIVITY ANALYSIS

To confirm our results we carried out sensitivity analysis changing the threshold for the risk group.

### 5% RISK THRESHOLD

At inclusion, high-risk patient are more likely to be prescribed the same therapeutic classes as in the reference analyze. We note the addition of Iron. Concerning molecules Amlodipine and Nicardipine still were more given to high-risk patients. Whereas in the low-risk group, there was the introduction of : **CEI + Diuretics, ARA2+ Diuretics, GLP-1 Like, Anti-Xa, Anti-Aggregant.**

Interestingly, at T+1 year, the difference in prescription in ICC, Insulin, Iron, and EPO carried over while in the reference analyze there were only **ICC and Insulin.**

Equally, at T+2 years, Amlodipin is still more prescribe in the high-risk group.

### 20% RISK THRESHOLD

At inclusion, high-risk patient are more likely to be prescribed the same therapeutic classes as in the reference analyze. We note the addition of Anti-psychotics.

While in low risk patients, **CEI, sulfamids, GLP-1 like, Vitamin K antagonist and Statins** are more prescribed. Interestingly, anti-gout are more prescribe at T+1 year.

# CONCLUSION

**Strengths**

•Real life data were used

•First time use of French data

•Granulometry of data

**Weaknesses**

•Lack of drug posologies

•Lack of hospitalisation frequencies

•Did not account for important unmeasured predictors

**Conclusion**

This study allowed us to assess risk evaluation for CKD. However, due to the lack of external validation the ND-CRIS score should not be used without validation.  Differences between the different groups are conform with the current guidlines of care.

# ABSTRACT

Background : Both diabetes and chronic kidney disease are a burden to health spendings. Avoiding complications of CKD such as dialysis is important. A better monitoring of at risk patients is therefore needed. Using risk-score to discriminate between high-risk patients and low-risk patients can be helpful to target the most vulnerable population.

Objective : We assessed the difference in drug prescription between high and low risk patients to evolve to terminal chronic kidney disease.

Methods : Using the french cohort ND-CRIS a 3-year prognosis score of evolution to terminal chronic kidney disease, was developed using a logistic regression model. The model was validated internally.

The population was then divided between high-risk and low-risk for a risk-threshold of 0,10. Using chi-2 tests, prescription drugs were compared between the two groups, in different time frame (inclusion, T+1 year, T+ 2 years). Time-evolution of prescription was also assessed. Sensitivity analyses were performed using different risk thresholds.

Results : At inclusion, differences were observed concerning prescriptions of anti-diabetes treatment such as insulin ($p = 0.012$) in high risk group, metformin ($p<0,0001$), gliclazid ($p=0,0065$), sitagliptin ($p=0,014$) in the low risk group. Concerning anti-hypertensive drugs difference exist : calcic canal inhibitors ($p=0,037$) are more prescribed in high risk patients.

Calcic canal inhibitors prescription differences substist at T+1 ($p=0,0151$), as well as insulin ($p=0,0025$), and metformin ($p=0,0318$). At T+2, the only difference is the prescription of amlodipin ($p=0,0003$).

In the whole cohort, prescription of opioids ($p=0,002$), glinids ($p=0,0037$), iron ($p=0,028$), acetaminophen($p=0,0011$) are increasing, while metformin, beta-blockers ($p=0,0009$), diuretic ($p < 0,0001$) and statins ($p=0,029$) are decreasing.

These results are confirmed in the sensitivity analyses.

Conclusion : Even unknowingly practitioners are differentiating prescription between the high risk group and the low risk group. Such differences indicate the possibility to personalize patient follow-up with no interference on quality of care.

# REFERENCES

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