ProFiL, a training-and-communication network program in nephrology for community pharmacists:

impact on knowledge, clinical competences, quality of medication use and clinical variables

Instituts de recherche en santé du Canada
Amgen Inc.
Léo-Pharma
Cercle du doyen
CKD a serious condition

- Prevalence of 12.5% in Canada (3.1% at stage 3-5)
- Prevalence of about 25% in patients with diabetes or hypertension
- Incidence of kidney failure doubled between 2000 and 2010

CKD patients
- Elderly (72 years old)
- Numerous health problems (5-6)
- Multiple medications (12)
- OTC use (80%)
- Many physicians (3.6 prescribers in 6 months)

High risk of drug-related problems (DRPs)
Management of CKD

- Objectives:
  - Prevent or control CKD complications
  - Slow the progression of kidney function decline

- Management
  - Control blood pressure, diabetes, and other CVD risk factors
  - Avoid nephrotoxic medications
  - Adjust medications based on kidney function
  - Monitor adherence to medications

- Predialysis clinic
  - Multidisciplinary team (physicians, nurses, dieticians...)
  - Pharmacists with expertise in nephrology
  - Involvement of pharmacists is limited
Community pharmacists

- Most accessible primary health care providers
  - ≥ 1 visit per month
  - Complete list of medications including OTC and natural products
  - They have the responsibility to detect DRPs and ensure appropriate medication use

BARRIERS
- Limited training in nephrology
- No access to important clinical information (eGFR)
- Undefined role within a multidisciplinary predialysis team
ProFiL Program

Training-and-communication program designed to improve the management of CKD by community pharmacists for patients followed in predialysis clinic

Conduct a cluster randomized trial to evaluate the ProFiL Program
Objectives

**Primary objective:**
- Compare the mean change in the quality of medication use in ProFiL and UC patients

**Secondary objectives:**
- Knowledge/clinical competences of community pharmacists
- Progression of the clinical variables (eGFR, blood pressure, HbA1C, LDL-c)
Study design

- Open-labelled, controlled, cluster-randomized clinical trial with 1 year follow-up

**6 predialysis clinics**
- Hôpital de la Cité-de-la-Santé
- Hôpital Maisonneuve-Rosemont
- Centre Hospitalier universitaire de Sherbrooke
- Hôpital Charles LeMoyne
- Hôpital Royal Victoria
- Jewish General Hospital

Predialysis clinics

Patients

Pharmacies / Pharmacists

ProFiL  Usual Care

2 ProFiL: 1 UC
Study population - patients

Patients
- Adult
- CKD
  - moderate (30-59 mL/min/1.73m²)
  - severe (15-29 mL/min/1.73m²)
- Have an eligible current pharmacy that agrees to participate
Study population - Pharmacies

**Pharmacies**

Adequate coverage by participating pharmacists:

- >250 prescriptions/day: at least 60h/wk
- OR
  - ≤ 250 prescriptions/day: at least 35h/wk
- OR
  - Pharmacies opened <7 days/week: at least 50% of opening hours
ProFiL Program

- Web-based interactive training
- Information exchange program
  Clinical summary
  List of medications
- Privilege access to pharmacists with expertise in nephrology
ProFiL program – Web-based training program

OBJECTIVES
- Familiarize pharmacists with a set of DRPs related to CKD (PAIR criteria)
- Proposed a systematic approach to detect and manage PAIR-DRPs

FORMAT
- 90 minutes
- 2 clinical vignettes (moderate/severe CKD)
Medication recorded in pharmacy chart

ProFil clinical summary

Clinical guide

OTC / NHP

Pharmacist with expertise in nephrology
Diagramme des 8 étapes

Cliquez sur « Débuter » lorsque vous êtes prêt à débuter celle-ci.

1. Vérifier les doses des médicaments au dossier.
2. Vérifier la concordance entre les listes de médicaments.
3. Évaluer l'adhésion au traitement.
4. Analyser les résultats de tension artérielle.
5. Analyser les résultats de glycémies.
6. Vérifier l'horaire d'administration réel des médicaments.
7. Déterminer le statut tabagique.
8. Déterminer si le patient prend des médicaments en vente libre et/ou des produits de santé naturels inadéquats.
Gestion des problèmes détectés
Remplir le formulaire d'opinion pharmaceutique

OPINION PHARMACEUTIQUE

MÉDECIN
D' / D

PATIENT
M. / Mme

RAMQ :

ÉVALUATION DE LA FONCTION RÉNALE

Clcr (mL/min) ou débit de filtration glomérulaire (mL/min/1,73m²) :

En date du :

PROBLÈME(S) OBSERVE(S)

☐ Ajustement posologique requis selon la fonction rénale pour :

☐ Médicament non recommandé selon la fonction rénale :

☐ Discordance significative entre le dossier-pharmacie et votre profil pharmaceutique pour :

☐ Non-adhésion (☐>120% ou ☐< 80% en 90 jours) à un médicament :

☐ Tension artérielle supérieure aux cibles visées :

☐ Épisodes d'hypoglycémie :

☐ Interaction médicamenteuse entre :

☐ Prise inadéquate d'un médicament :

☐ Référence requise pour un traitement ou un suivi anti-tabagique :

☐ Traitemen inadéquat avec un médicament en vente libre :

☐ Traitement inadéquat avec un produit de santé naturel :

☐ Autre problème :

Table des matières
Quality of medication use -PAIR criteria

- 51 clinically significant DRPs for CKD patients requiring the intervention of community pharmacists when detected

- RAND appropriateness process (3 rounds)
  - 4 nephrologists
  - 2 family physicians
  - 4 nephrology pharmacists
  - 2 community pharmacists

- Validation using pilot data:
  - Inter-rater reliability: Kappa: 0.82-0.96; ICC: 0.93
  - Test-retest reliability: Kappa: 0.74-1.00; ICC 0.91
  - Conceptual validity
    - Expert judgment : 3.5 DRPs/patient
    - PAIR criteria: 2.5 DRPs/patient
Evaluation

- One year prior and after the recruitment

- Quality of medication use (PAIR criteria)
  - Documentation:
    - Pharmacy chart
    - ProFiL clinical summary
    - Patient interview (OTC and NHP)
  - Two evaluators + consensus if needed

- Clinical variables
  - Results available in predialysis clinic chart

- Knowledge/clinical competences
  - 10 questions (knowledge) and 2 clinical vignettes
Analyses

- Intent-to-treat approach
- Missing data at T12 were replaced by baseline scores/group mean
- Multivariate linear mixed effects model to take into account the clustering of data within pharmacy and patient-level intra-correlation induced by repeated measures
- To adjust for confounders, all variables statistically significant (p < 0.2) in a bivariate model including the study group were included in the final multivariate model if they remained statistically significant (p < 0.1).
412 pharmacies (931 pharmacists)
1732 patients solicited

207 pharmacies (494 pharmacists)
442 patients participated

ProFil

Usual Care

Lost to follow-up:
0 pharmacy
28 pharmacists\(^b\)
16 patients\(^c\)

Withdrawal:
3 pharmacies
22 pharmacists\(^d\)
0 patient

Death:
0 pharmacist
19 patients

139 pharmacies
345 pharmacists
304 patients

139 pharmacies
345 pharmacists
304 patients

Pharmacies:
Declined to participate (n = 205)

Pharmacists:
Decline or not eligible (n = 437)

Patients:
Not meeting inclusion criteria\(^a\) (n = 684)
Declined to participate (n = 198)
Pharmacy declined to participate (n = 408)

Lost to follow-up:
0 pharmacy
6 pharmacists\(^b\)
10 patients\(^c\)

Withdrawal:
1 pharmacy
0 pharmacist
1 patient

Death:
0 pharmacist
10 patients

168 pharmacies
345 pharmacists
304 patients

68 pharmacies
149 pharmacists
138 patients

Lost to follow-up:
0 pharmacy
28 pharmacists\(^b\)
16 patients\(^c\)

Withdrawal:
3 pharmacies
22 pharmacists\(^d\)
0 patient

Death:
0 pharmacist
19 patients

139 pharmacies
345 pharmacists
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68 pharmacies
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0 pharmacy
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3 pharmacies
22 pharmacists\(^d\)
0 patient

Death:
0 pharmacist
19 patients

\(^a\) Patient not meeting inclusion criteria: eGFR < 15mL/min/1.73m\(^2\) (n=325); eGFR ≥ 90mL/min/1.73m\(^2\) (n=97); doesn’t have Quebec health insurance plan (n=91); unable to manage their medication (n=55); unable to speak English or French (n=49); withdrawal before entering the study (n=26); client of more than one pharmacy (n=19); unable to understand the study (n=19); and hospitalized (n=4).

\(^b\) Changed pharmacy (n=34).

\(^c\) Changed pharmacy (n=10); withdrawal of their pharmacy (n=9); and dialysis (n=7).

\(^d\) Lack of time (n=17); withdrawal of pharmacy (n=3); and unsatisfied (n=2).
## Participants characteristics

<table>
<thead>
<tr>
<th></th>
<th>ProFiL n=304</th>
<th>Usual Care n=138</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Age (years): mean (SD)</strong></td>
<td>72 (12)</td>
<td>71 (13)</td>
</tr>
<tr>
<td><strong>Men: n (%)</strong></td>
<td>179 (59)</td>
<td>83 (60)</td>
</tr>
<tr>
<td><strong>Severity of renal disease (Grade 4): n (%)</strong></td>
<td>202 (67)</td>
<td>85 (62)</td>
</tr>
<tr>
<td><strong>eGFR (mL/min/1.73m²): mean (SD)</strong></td>
<td>27 (9)</td>
<td>28 (11)</td>
</tr>
<tr>
<td><strong>Comorbidities: n (%)</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Hypertension</td>
<td>283 (95)</td>
<td>130 (95)</td>
</tr>
<tr>
<td>Dyslipidemia</td>
<td>223 (75)</td>
<td>100 (74)</td>
</tr>
<tr>
<td>Type I diabetes</td>
<td>11 (4)</td>
<td>4 (3)</td>
</tr>
<tr>
<td>Type II diabetes</td>
<td>160 (54)</td>
<td>65 (48)</td>
</tr>
<tr>
<td>Anemia</td>
<td>160 (55)</td>
<td>77 (58)</td>
</tr>
<tr>
<td>Phosphocalcic metabolism disorder</td>
<td>138 (48)</td>
<td>60 (46)</td>
</tr>
</tbody>
</table>

|
Participants characteristics

<table>
<thead>
<tr>
<th>Pharmacies</th>
<th>ProFiL n = 139</th>
<th>Usual care n = 68</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Number of prescriptions per day</strong>: mean (SD)</td>
<td>440 (236)</td>
<td>458 (246)</td>
</tr>
<tr>
<td><strong>Pharmacy size (&gt;5000 ft²) : n (%)</strong></td>
<td>75 (61)</td>
<td>37 (62)</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Pharmacists</th>
<th>n = 345</th>
<th>n = 149</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Women: n (%)</strong></td>
<td>236 (68)</td>
<td>100 (67)</td>
</tr>
<tr>
<td><strong>Salaried pharmacist: n (%)</strong></td>
<td>250 (73)</td>
<td>110 (74)</td>
</tr>
</tbody>
</table>
Knowledge and clinical competences

- **Knowledge score (%)**
  - ProFiL: 75.2, 83.5, 8.2
  - Usual Care: 75.6, 79.2, 3.6
  - Adjusted difference: 5.3% (95%CI: 2.2 to 8.4)
  - Adjusted for having a training on pharmaceutical opinion in the last year and for being an associate clinician

- **Competencies score (%)**
  - ProFiL: 49.2, 58.7, 9.5
  - Usual Care: 48.8, 50.9, 2.2
  - Adjusted difference: 7.3% (95%CI: 4.1 to 10.6)
  - No significant confounding variables
Quality of pharmacotherapy

Δ DRPs/patient

Adjusted difference* -0.53 DRPs (95%CI: -0.96 to -0.10)

* Adjusted for patient education and pharmacist working in several pharmacies
## Number of DRPs per patient

<table>
<thead>
<tr>
<th>PAIR DRPs</th>
<th>Mean change (95% CI)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>ProFiL</td>
</tr>
<tr>
<td>Inappropriate prescription:</td>
<td></td>
</tr>
<tr>
<td>Incorrect dosage</td>
<td>-0.10 (-0.17 to -0.03)</td>
</tr>
<tr>
<td>Contraindicated agent</td>
<td>-0.15 (-0.21 to -0.08)</td>
</tr>
<tr>
<td>Nonoptimal treatment adherence</td>
<td>-0.10 (-0.22 to 0.03)</td>
</tr>
<tr>
<td>Nonoptimal blood pressure</td>
<td>-0.09 (-0.14 to -0.04)</td>
</tr>
<tr>
<td>Hypoglycemia secondary to sulfonylurea</td>
<td>0.04 (0.00 to 0.07)</td>
</tr>
<tr>
<td>Drug interaction</td>
<td>0.00 (-0.02 to 0.04)</td>
</tr>
<tr>
<td>Drug used inappropriately</td>
<td>-0.08 (-0.13 to -0.03)</td>
</tr>
<tr>
<td>Smoking</td>
<td>0.00 (-0.02 to 0.04)</td>
</tr>
<tr>
<td>Inappropriate use of</td>
<td></td>
</tr>
<tr>
<td>Over-the-counter medication</td>
<td></td>
</tr>
<tr>
<td>Naturel health product</td>
<td>-0.11 (-0.17 to -0.04)</td>
</tr>
<tr>
<td></td>
<td>0.00 (0.00 to 0.00)</td>
</tr>
</tbody>
</table>
# Progression of clinical variables

<table>
<thead>
<tr>
<th></th>
<th>ProFiL Study entry (T0) Mean (SD)</th>
<th>ProFiL Changement during study (T12-T0) Mean (95% CI)</th>
<th>Usual Care (UC) Study entry (T0) Mean (SD)</th>
<th>Usual Care (UC) Changement during study (T12-T0) Mean (95% CI)</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>eGFR (mL/min/1.73m2)</strong></td>
<td>26.8 (9.3)</td>
<td>0.2 (-2.3 to 2.7)</td>
<td>28.2 (10.6)</td>
<td>-1.3 (-2.4 to -0.2)</td>
</tr>
<tr>
<td><strong>Blood pressure (mmHg)</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Systolic</td>
<td>135.8 (19.4)</td>
<td>-1.4 (-3.5 to 0.8)</td>
<td>136.4 (20.2)</td>
<td>-0.3 (-3.9 to 3.3)</td>
</tr>
<tr>
<td>Diastolic</td>
<td>69.4 (11.6)</td>
<td>-0.4 (-1.7 to 0.8)</td>
<td>70.7 (11.5)</td>
<td>-1.0 (-3.0 to 0.9)</td>
</tr>
<tr>
<td><strong>LDL cholesterol (mmol/L)</strong></td>
<td>2.0 (0.7)</td>
<td>-0.1 (-0.2 to 0.0)</td>
<td>2.0 (0.7)</td>
<td>0.0 (-0.1 to 0.1)</td>
</tr>
<tr>
<td>Patients with dyslipidemia</td>
<td>1.9 (0.7)</td>
<td>-0.1 (-0.2 to 0.0)</td>
<td>2.0 (0.7)</td>
<td>-0.1 (-0.2 to 0.0)</td>
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</tr>
<tr>
<td><strong>Glycosylated hemoglobin (%)</strong></td>
<td>6.9 (1.3)</td>
<td>0.0 (-0.1 to 0.1)</td>
<td>6.7 (1.1)</td>
<td>0.1 (-0.1 to 0.2)</td>
</tr>
<tr>
<td>Patients with diabetes</td>
<td>7.4 (1.4)</td>
<td>-0.1 (-0.3 to 0.1)</td>
<td>7.1 (1.4)</td>
<td>0.2 (-0.1 to 0.5)</td>
</tr>
</tbody>
</table>
Summary of results

- Quality of medication use improved significantly in the ProFiL group
  - Incremental reduction of 0.5 DRP/patient
  - Significant reduction of DRPs related to:
    - Inappropriate dosage adjustment
    - Drug not recommended in CKD
    - Uncontrolled blood pressure control
    - Inappropriate use
    - OTC not recommended

- After one year, persistent improvement in knowledge (5%) and clinical competencies (7%) of community pharmacists

- No significant differences on the change in eGFR, blood pressure, HbA1C, and LDL-cholesterol.
Quality of medication use

- Quality of medication use is suboptimal (2 DRPs/pt)
  - Regular follow-up in predialysis clinic
  - Multidisciplinary team

- Training/support + essential clinical information = improvement
Strengths and limits

**Strengths**
- Cluster-randomization ➞ high level of internal validity
- Relatively high participation rate
  - Pharmacies’ acceptance: 50%
  - Patients’ refusal: 11% (of patients invited)
- DRPs were blindly evaluated using validated criteria

**Limits**
- Recruitment of patients after randomisation (selection bias)
- Low questionnaire response rate at T12 (65%)
- Missing values for laboratory test results
- Only few patients per pharmacy
Next step….

- Adapt and implement ProFiL to improve the management of CKD patients followed in primary care

- Take into account recent legislation changes
  - Dossier Santé Québec
  - Bill 41: adapt prescription, prescribe laboratory tests

- External facilitator/expert pharmacist to accelerate clinical practice changes
Thanks!

Nephrologists
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Martine LeBlanc
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  - Patricia Sauvé
  - François Ste-Marie
  - Paradis

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Nephrology pharmacists: **Anne Lord** and Robert Bell

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