Pharmaco-epidemiological outcome research

Using the PHARMO-Eindhoven Cancer Registry linkage

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Eindhoven Cancer Registry

• Area of 2.4 million inhabitants
• 10 hospitals
• 2 radiotherapy institutes
• 20,000 new cancer diagnosis/year (including BCC)

• Part of Netherlands CR
• 100% coverage
Eindhoven Cancer Registry
since 1955

- Comorbidity since 1995 (Charlson Index)
- Tumor stage, grade
- Treatment
  - surgery
  - radiotherapy
  - systemic therapy
- Sex, age, SES
- Survival
Diabetes and cancer: 1 in 10
Diabetes and cancer: 1 in 5

- 1990: 265,000
- 2000: 400,000
- 2010: 600,000
- 2020: 920,000

Bar chart showing the increase in diabetes and cancer cases from 1990 to 2020.
Impact of DM on treatment and survival of cancer patients

- 2007:
- Population-based analyses
- Cancer diagnosis 1995-2002
- 5,555 cancer patients with Diabetes Mellitus (DM)
- 52,943 cancer patients without DM

Worse overall survival

Eindhoven Cancer Registry

since 1955

**PHARMO:**
Linkage with pharmacy data from public and hospital pharmacies
PHARMO data
# ECR-PHARMO study population ‘98–’11

<table>
<thead>
<tr>
<th></th>
<th>1998-2011 (N=91,540)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>n (%)</td>
</tr>
<tr>
<td><strong>Gender</strong></td>
<td></td>
</tr>
<tr>
<td>Male</td>
<td>48,397 (53)</td>
</tr>
<tr>
<td>Female</td>
<td>43,143 (47)</td>
</tr>
<tr>
<td><strong>Age at tumor diagnosis</strong></td>
<td></td>
</tr>
<tr>
<td>≤ 49</td>
<td>11,838 (13)</td>
</tr>
<tr>
<td>50 – 59</td>
<td>15,652 (17)</td>
</tr>
<tr>
<td>60 – 69</td>
<td>25,321 (28)</td>
</tr>
<tr>
<td>70 – 79</td>
<td>25,932 (28)</td>
</tr>
<tr>
<td>≥ 80</td>
<td>12,797 (14)</td>
</tr>
<tr>
<td><strong>Cancer sites</strong></td>
<td></td>
</tr>
<tr>
<td>Skin, Basal Cell Carcinoma</td>
<td>21,026 (23)</td>
</tr>
<tr>
<td>Breast</td>
<td>10,625 (12)</td>
</tr>
<tr>
<td>Colon and Rectum</td>
<td>10,005 (11)</td>
</tr>
<tr>
<td>Lung, Bronchus and Trachea</td>
<td>9,246 (10)</td>
</tr>
<tr>
<td>Prostate</td>
<td>8,155 (9)</td>
</tr>
<tr>
<td>Skin</td>
<td>7,000 (7)</td>
</tr>
<tr>
<td>Haematolymphopoietic</td>
<td>5,356 (6)</td>
</tr>
<tr>
<td>Not further specified</td>
<td>20,127 (22)</td>
</tr>
</tbody>
</table>
Can a Diabetes Drug Prevent Cancer Death?

By James Saftig

With its near-perfect safety record, low cost, and favorable side-effect profile, the anti-diabetic drug metformin is one of the few FDA-approved drugs Life Extension® recommends its members should take every day.

Between 1990 and 2011 alone, over 1,000 published studies have yielded confirmatory data on its numerous anti-aging properties, from weight loss and glucose control to cardiovascular disease and cancer defense.

As the medical establishment continues to ignore this mounting body of evidence, ongoing research powerfully validates our position.

In one of the largest studies of its kind, a team of scientists analyzed cancer risk among 8,000 diabetics treated with metformin. Over a 10-year period, they observed a 54% lower incidence of all cancers compared to the general population.

Metformin not only exerted a major protective effect against cancer development, but those who developed cancer exhibited a significantly higher survival rate, including those with malignant cancers of the lung, colon, and breast. Of equal significance was the finding that the earlier the metformin regimen was initiated, the greater the preventive benefit.

Given that diabetics are predisposed to a horrifically wide array of cancers—or the breast, colon, liver, pancreas, kidney, endometrium (uterine lining), among others—these results have profound implications for all maturing individuals.

In this article, the most recent data supporting metformin’s anti-cancer mechanisms are detailed. You will learn of its specific mechanisms of action, which shed further light on the link between obesity, diabetes, and cancer initiation. You will also be introduced to several other anti-diabetes therapies that may also possess anti-cancer properties.
### Colorectal cancer cohort ECR-PHARMO ’98–’10

<table>
<thead>
<tr>
<th>Medication at cancer diagnosis</th>
<th>Colorectal cancer (n=7,794)</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Diabetes medication</strong></td>
<td></td>
</tr>
<tr>
<td>Metformin</td>
<td>6%</td>
</tr>
<tr>
<td>Insulin</td>
<td>3%</td>
</tr>
<tr>
<td>Sulfonylureas</td>
<td>7%</td>
</tr>
<tr>
<td>Thiazolidinediones</td>
<td>1%</td>
</tr>
<tr>
<td><strong>Other medication</strong></td>
<td></td>
</tr>
<tr>
<td>Statins</td>
<td>18%</td>
</tr>
<tr>
<td>Platelet aggregation inhibitors</td>
<td>21%</td>
</tr>
</tbody>
</table>
Association between metformin use started *after* colorectal cancer and mortality - No drug effect, solely confounding by indication?


**ECCO Amsterdam 29-09-2013**
Aim

- To assess whether, and to which extent, use of metformin started after the diagnosis of colorectal cancer (CRC) is associated with an increased overall survival compared with use of sulfonylurea derivatives (SU)
Study design

ECR/PHARMO region
Colorectal cancer (CRC)
Years of diagnosis 1998-2010
TNM stage I, II, III and IV
(n=7,794)

User of glucose lowering drugs
(n=1,247)

Follow-up of 6 months prior to CRC diagnosis
(n=1,147)

User of glucose lowering drugs after CRC diagnosis
(n=1,091)

Incident user of glucose lowering drugs
(n=337)

Started with metformin monotherapy
(n=164)

Started with sulfonylurea derivatives monotherapy
(n=108)

No glucose lowering drugs
(n=6,547)

Follow-up of less than 6 months prior to CRC diagnosis
(n=100)

User of glucose lowering drugs before CRC diagnosis only
(n=56)

Prevalent user of glucose lowering drugs
(n=758)

Started with another (combination of) glucose lowering drugs
(n=65)
Still a wonder drug?

Survival (%)

Time since the start of diabetes medication (months)

Metformin
Sulfonylurea derivatives

Log-rank test: p=0.02
Results

Overall mortality of CRC patients starting on metformin (n=164) compared with those starting on sulfonylurea derivatives (n=108)

\[ HR_{\text{drug} \times \text{cumulative exposure}} (95\% CI) : 1.03 (0.99-1.06) \]
Discussion

• 59% lower hazard for overall mortality at baseline for CRC patients starting on metformin compared to on sulfonylurea derivatives.

• This advantageous effect of seemed to disappear with duration of exposure to the drug.

• These findings suggest that
  • metformin users have favourable characteristics at baseline
  • During follow-up, the remaining selection of the fittest patients with sulfonylurea derivatives and the disease progression of diabetes may have result in a disappearing metformin effect
Eindhoven Cancer Registry development since 1955

PRO’s:
Longitudinal lifestyle evaluation and Patient Reported Outcomes
Methods: ECR sampling frame

- Patient characteristics
- Tumor characteristics
- Treatment
- Alive? (linkage municipal registry)
PROFILES Registry

- **Patient Reported Outcomes Following Initial treatment and Long-term Evaluation of Survivorship** *
- Infrastructure for data collection: web-based and paper
- Longitudinal survey data linked to cancer registry data

- [www.profielstudie.nl](http://www.profielstudie.nl) for patients
- [www.profilesregistry.nl](http://www.profilesregistry.nl) for researchers (free access to data for academic users)

* Van de Poll-Franse, Eur J Cancer 2011
Over Profiel

Profiel is wetenschappelijk onderzoek naar kwaliteit van leven bij mensen die kanker hebben of hebben gehad. Hiervoor werken onderzoekers van het Integraal Kankercentrum Zuid (IKZ) in Eindhoven en de Universiteit van Tilburg (UvT) samen met medisch specialisten van ziekenhuizen in Noord-Brabant en Limburg.

Doel
Het doel van Profiel is om meer te weten te komen over de gevolgen van kanker voor het leven van mensen die kanker hebben of hebben gehad. De resultaten van het onderzoek dragen bij aan een betere (na)zorg voor patiënten.

Sinds 2004
Profiel komt voort uit een langer lopende onderzoekslijn naar kwaliteit van leven in de regio Zuid-Nederland. Sinds 2004 is er bij meer dan 8000 (ex-)kankerpatiënten onderzoek gedaan naar de late gevolgen van kanker, zorggebruik, en maatschappelijke implicaties.

Resultaten
De resultaten van deze onderzoeken worden besproken met medisch specialisten uit de regio. Bovendien worden de resultaten gepubliceerd in (inter-)nationale tijdschriften. Tevens worden presentaties gehouden op (inter-)nationale congressen en workshops georganiseerd waarin de resultaten besproken worden.

Lees meer over wie we zijn, wat we doen en wie mee doen.

* Profiel is de vertaling van PROFILES dat staat voor Patient Reported Outcomes Following Initial treatment and Long term Survivorship

Nieuws

10 Jaar na Hodgkin Lymfoom: betere kwaliteit van leven

EINDHOVEN – Patiënten bij wie 10 tot 15 jaar geleden de diagnose Hodgkin lymfoom is vastgesteld hebben een betere kwaliteit van leven dan patiënten bij wie 5 tot 9 jaar geleden de diagnose Hodgkin lymfoom is vastgesteld. Beide groepen hebben echter een betere kwaliteit van leven dan bij patiënten bij wie zo'n 10 jaar geleden de diagnose was gedaan. Dit blijkt uit onderzoeken van de afdeling Interdisciplinair Kankercentrum Zuid (IKZ) en de Universiteit van Tilburg (UvT).
Data Archive Homepage

Please select one of the following links to start accessing the Profiles Registry data and metadata.

To download data you have to be logged in. If you do not have a user account yet, click here to apply for one.

Getting Started
Information about the Data Archive for first time users.

Login
Login to download datasets. No account yet? Click here.

Browse Studies
View all studies.

Browse Topics
View all studies and publications by topic.

Browse Concepts
View the concepts used in Profiles Registry.

www.profilesregistry.nl
Chemotherapy-Induced Neuropathy and Its Association With Quality of Life Among 2- to 11-Year Colorectal Cancer Survivors: Results From the Population-Based PROFILES Registry

Floortje Mols, Tonneke Beijers, Valery Lemmens, Corina J. van den Hurk, Gerard Vreugdenhil, and Lonneke V. van de Poll-Franse

ABSTRACT

Purpose
To gain insight into the prevalence and severity of chemotherapy-induced neuropathy and its influence on health-related quality of life (HRQOL) in a population-based sample of colorectal cancer (CRC) survivors 2 to 11 years after diagnosis.

Methods
All alive individuals diagnosed with CRC between 2000 and 2009 as registered by the Dutch population-based Eindhoven Cancer Registry were eligible for participation. Eighty-three percent (n = 1,643) of patients filled out the European Organisation for Research and Treatment of Cancer (EORTC) Quality of Life Questionnaire (QLQ) C30 and the EORTC QLQ Chemotherapy-Induced Peripheral Neuropathy 20.
Chemotherapy-induced neuropathy

- Increasing number of colorectal cancer (CRC) survivors
- Many of them face continuing problems like chemotherapy-induced peripheral neuropathy (CIPN)
- CIPN may negatively impact quality of life but;
  - studies are scarce and
  - mostly focus on acute CIPN
Response and patient characteristics

• **Response:**
  Questionnaire was completed by 1648 CRC survivors (83% response rate)

• **Patient characteristics:**
  • 56% male
  • 59% colon cancer
  • Mean age 69 years
  • Mean time since diagnosis 6 years
  • 31% (n=500) was treated with chemotherapy
Mean symptom score

**Colon Cancer**

- No chemo: 8
- Chemo without oxaliplatin: 13.2
- Oxaliplatin: 15.3

- Sensory scale

**Rectal Cancer**

- No chemo: 8.5
- Chemo without oxaliplatin: 8.2
- Oxaliplatin: 13.3

- Sensory scale

- P=0.032
1 in 3 patients treated with oxaliplatin reports up to 10 years after diagnosis (!) tingling, painful hands or feet with big impact on QoL!
Clinical implications

• Clinical implications:
  • No well-accepted proven therapy to prevent CIPN.

• Future studies should:
  • Focus on ways to prevent or alleviate CIPN

• But also: what is the added value of oxaliplatin in adjuvant setting (current stage II/III disease)?!
  • Overall survival vs. long-term symptoms & quality of life
Health-Related Quality of Life and persisting symptoms in relation to (R-)CHOP14 (R-)CHOP21 among Patients with Diffuse Large B-Cell Lymphoma in the Netherlands
932 patients diagnosed and registered with DLBCL between 1/1/2004 and 1/1/2010 and living in the region of CCCS.

469 eligible patients (i.e. older than 18 years at diagnosis and still alive at time of questionnaire mailing).

Specialists’ from 18 hospital locations received an invitation letter to participate in the study.

Addresses for the remaining 322 patients were checked for accuracy.

293 patients received a questionnaire.

250 patients returned a completed questionnaire (85%).

Refusal of 2 general hospitals and 2 locations containing 110 patients in total.

Exclusion of 15 patients (because of other medical problems) on advice of the specialists.

22 patients not registered in PHAROS yet.

29 unverifiable addresses.

43 patients did not complete the questionnaire.
Patient characteristics

R-CHOP14 vs. R-CHOP21

In comparison with R-CHOP14 (n=93) patients, R-CHOP21 (n=126) patients are on average:

• A bit older: 67 vs. 61 jaar (p<0.01)
• Longer after diagnosis: 2.9 vs. 2.0 jaar (p<0.01)
• Better stage distribution: more stage I (44% vs. 16%) en less often stage IV (16% vs. 26%)
R-CHOP14 vs. R-CHOP21

Percentage patients that report symptoms

<table>
<thead>
<tr>
<th>Symptom</th>
<th>R-CHOP14</th>
<th>R-CHOP21</th>
</tr>
</thead>
<tbody>
<tr>
<td>Tingling hands/feet</td>
<td>43%</td>
<td>29%</td>
</tr>
<tr>
<td>Fatigue</td>
<td>47%</td>
<td>35%</td>
</tr>
</tbody>
</table>
Clinical implications

• R-CHOP14 results in almost similar HRQoL scores as compared to R-CHOP21
• BUT… more neuropathy and fatigue
• Recent phase 3 studies showed no improved survival between patients treated with R-CHOP14 vs R-CHOP21*
• Doctors should pay attention to persisting symptoms: at least 1/3 experiences persisting neuropathy and/or fatigue
• And again: what is the added value of the R-CHOP14 scheme?!?!

Cancer Registry data
+ pharmacy data
+ patient reported outcomes

Comprehensive approach
• Continuous monitoring of (long term) impact of cancer and (new) therapies
• Contribute to the discussion on the added value of (new) therapies in daily clinical practice

▶ Improve quality of (cancer) care!
Other examples of ECR-PHARMO Linkage

1. β-Blocker use and all-cause mortality of melanoma patients: Results from a population-based Dutch cohort study. Eur J Cancer. 2013
www.pharmo.nl
www.ikz.nl
www.profilesregistry.nl