

Comparing routinely collected population level healthcare data to a prospective clinical study of Wilms Tumour in England

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1. Introduction

Accurately curated routinely collected healthcare data (RCD) provides real-world, representative information across large populations over an extended follow-up period [1]. This is challenging to achieve using dedicated research studies, especially for rare diseases such as paediatric cancers.

47% of National Institute for Health Research (NIHR) funded randomised controlled trials in the UK planned to use RCD, however very few of these were in paediatric oncology [2]. Greater adoption of RCD in oncology research requires confidence in the fidelity of the data collected and minimising barriers to using it.

In England, the National Cancer Registration and Analysis Service (NCRAS) Get Data Out (GDO) programme uses RCD such as hospital episode statistics, chemotherapy and radiotherapy administration records and community prescription data, to provide anonymised statistics on incidence, route to diagnosis, treatment modalities used [3], and overall survival for English residents diagnosed with cancer at any age. To reduce the risk of de-anonymisation, externally published data groups must contain at least approximately 100 cases a year. Consequently, there are very few paediatric groupings, but within kidney cancer, data on all Wilms tumours (WT) are detailed as a separate entity.

We compared the GDO data with IMPORT (Improving Population Outcomes of Renal Tumours of childhood) a prospective study of paediatric renal tumours in the UK [4]. IMPORT opened at 19 of the 20 principal treatment centres treating paediatric cancers in the UK from

late 2012 onwards. The remaining centre treats mainly adolescents, an age group where WT is very rare, but cooperated with a nearby paediatric centre to register and treat any relevant patients with WT. The IMPORT study was amended in 2019 to support participation by UK centres in the “UMBRELLA” study – a prospective clinical observational study of the International Society of Paediatric Oncology (SIOP) Renal Tumour Study Group [5].

2. Methods

The IMPORT study database was accessed on 29/06/2023 in accordance with study information governance. Analysis was limited to English-resident children with a new diagnosis of WT diagnosed between 1/1/2014 and 31/12/2018 (all full calendar years when the study was open to registration at all childhood cancer principal treatment centres in England).

GDO data were downloaded from <https://www.cancerdata.nhs.uk/getdataout/kidney> (releases GDO_0031 and GDO_0030). Analysis was performed in R using the *readxl*, *tidyverse* and *survival* packages.

3. Results

Of a total 727 cases in IMPORT, 417 were enrolled from English centres in 2014–18. After exclusion of 9 non English-resident cases and 2 enrolled at relapse, 345/406 (85%) had a diagnosis of WT (323 unilateral and 22 bilateral). GDO published 442 patients of all ages diagnosed with

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Table 1

Comparison of percentage enrolment in clinical trials of WT to population level national registry.

Period	Study	Proportion of National registry cases within study
1/1980–12/1985	UKW1	81%
1/1986–9/1991	UKW2	88%
10/1991–3/2001	UKW3	94%
3/2002–12/2005	SIOP 2001	92%
1/2014–12/2018	IMPORT	80% ^a

^a Data inferred based on 98% WT cases in GDO (i.e. n = 433) being in cases aged 0–19 yrs.

WT in the same 5 yr period. A paediatric age range (0–19 yrs) is not published separately due to small number restrictions being applicable to WT in adults. However, an analysis performed within the NCRAS secure research environment showed that 98% of WT cases in the GDO were in patients aged 0–19 years. Hence, we estimate the proportion of children and adolescents diagnosed with WT in England who were registered in IMPORT to be 80% (Table 1). This is lower than in previous clinical studies of paediatric WT (spanning the period 1986–2005), where clinical trial participation was directly annotated in the national children’s tumour registry [6].

For the IMPORT cohort, data was available on the use of radiotherapy in 87.5% cases, chemotherapy 99.1% and surgery for all. GDO reported treatment data for 440/442 (99.5%) cases.

The use of combined treatment modalities was similar between IMPORT and GDO datasets (Fig. 1). Most common were chemotherapy and surgery (57.6% IMPORT cases vs 49.5% in GDO) and chemotherapy, surgery and radiotherapy (41.0% vs 42.0% respectively). In GDO, 3.6% were recorded as having surgery only and 0.9% chemotherapy and radiotherapy (without surgery), but no patient in IMPORT had these approaches. 2.5% were recorded as having chemotherapy only in GDO, with just 1 case in IMPORT.

Overall survival in GDO is provided as point estimates for 1- and 3-year cohorts. Comparing the period with the longest follow-up (2014–2016), 4 yr overall survival rates were 92.6% [95%CI 89.1–96.3%] for IMPORT and 93.4% [95%CI: 89.7–95.8%] for GDO (Fig. 2).

4. Discussion

This is the first study to compare national population-level RCD of renal tumours with a prospective clinical study of children with WT. We found similar treatment modalities and survival outcomes, with any differences likely due to age inclusion criteria and/or data fidelity (e.g. incomplete data coverage of treatment records). We recommend similar studies with other paediatric cancers and further work with GDO data to assess data linkage quality and classification. Aggregating GDO cases into 5-year cohorts would mitigate small-number publication restrictions.

The causes for the reduced enrolment rates on IMPORT are likely multifactorial and beyond the scope of this study. More widespread use of RCD in paediatric oncology research may mitigate against this loss of data capture, but several challenges remain. First, data access can be difficult, with multiple different approvals required to access data held by one organisation to be used by another for a secondary purpose. Whilst this was achieved rapidly and effectively when testing treatments for COVID19 in the RECOVERY trial [7], other groups doing non-COVID related studies have found the existing governance structures complex, arduous and slow [8].

Second, techniques used to aggregate data in published anonymised datasets such as GDO can preclude paediatric-specific research. For example, neuroblastoma, whilst having a similar incidence to WT, is not



Fig. 2. Aggregated Kaplan Meier overall survival for the 3 year time period with longest follow up (2014–2016) n = 214 for IMPORT and n = 271 for GDO. Data are yearly point estimates with 95% CI.

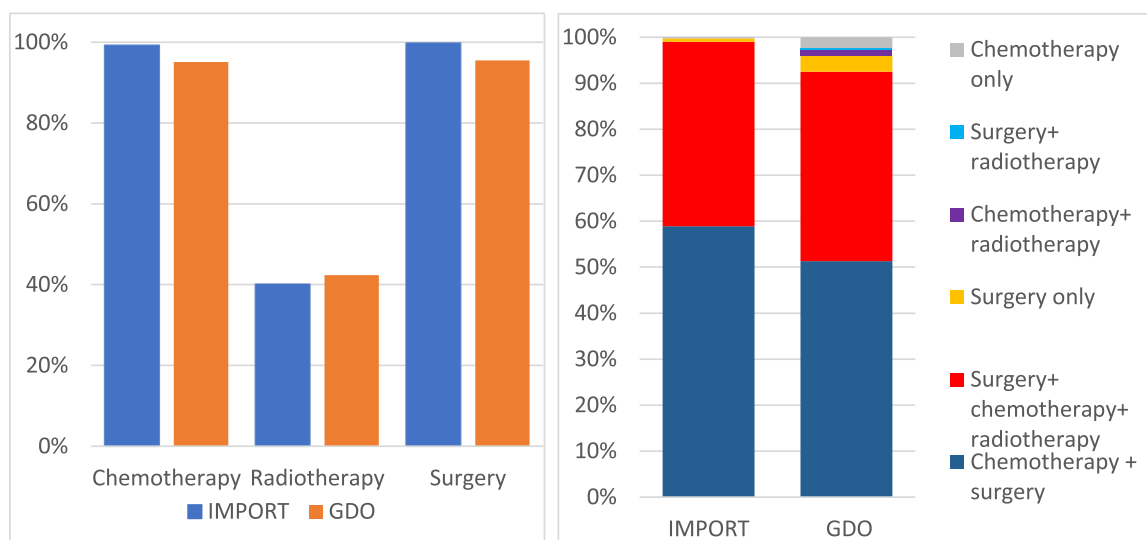


Fig. 1. Treatment modalities used. Left panel: Total use of each treatment modality, right panel: relative proportions of combined treatment modalities. N = 440 for GDO and n = 345 for IMPORT.

listed as a separate entity, and brain tumours are not presented by histological subtype.

Third, collection of population level RCD may be easier in a single provider system such as the English National Health Service, than multiple provider systems in other countries.

Fourth, the amount of data made publicly available is relatively limited and is not yet sufficient to either replace or supplement existing studies such as IMPORT.

These challenges could be addressed by large healthcare data holders increasing the amount of data they share in aggregated anonymised datasets and supporting access to more granular pseudoanonymised data in trusted research environments. Harmonising approaches to RCD collection will be important for the international collaborative studies common in paediatric oncology to harness their full potential.

CRedit authorship contribution statement

KPJ conceived the study. TJJ analysed the data and drafted the manuscript. ALC, RA-S, GV, TC and KPJ are responsible for IMPORT study data acquisition, and SV, LI and CS for the Kidney GDO data. All authors contributed to the revision of the manuscript.

Declaration of Competing Interest

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

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