Real-world EQ-5D-5L utility values in patients with melanoma derived using a digital 'bring your own device' platform

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BACKGROUND

Melanoma

Melanoma is an aggressive form of skin cancer that originates from melanocytes in the basal layer of the epidermis.

Although melanoma most frequently occurs on the skin[1], it can also arise in the mucous membranes of the mouth and genitalia, the respiratory, gastrointestinal, and uveal tracts and the leptomeninges.

Melanoma is the fifth most common cancer in the UK, with 14,509 new cases registered across the UK in 2014[2].

The incidence is rising, especially in older adults – about half of melanoma cases each year are in people aged 65 years and over.

However, melanoma also occurs relatively frequently in younger people (in contrast to most types of cancer): about one-quarter of melanomas in the UK between 2011 and 2013 were in patients aged younger than 50 years[2].

New treatments in melanoma are gradually transforming the disease into a chronic condition:

- For advanced disease stages, the median survival has significantly increased (from 9 months in stage 4 patients with limited treatment options, to a 3-year survival rate of up to 58%[3], with a proportion of them living to 5–10 years).
- In the early setting, adjuvant therapy is taking a prominent place in the therapeutic landscape, with many patients with normal life expectancies being exposed to treatments with potential side effects (some long term or irreversible).

The value of real-world data

Real-world data are vital to understand the impact of a chronic condition such as melanoma, and its treatments, on patients' lives, symptoms, functioning, work and other forms of productivity and daily activities, such as caring for a family.

The NICE methods guide[4] recommends collection of real-world data as a condition of entry into the revised Cancer Drugs Fund (CDF), to address uncertainty in technology appraisal.

In the real-world setting, data can be collected from a broader range of patients than is encountered in clinical trials, including those with co-morbidities and across all age ranges.

In the UK, melanoma patients are registered at the population level by one of the four National Cancer Registries and numerous regional melanoma registries; however, none of the existing registries collects health-related quality of life (HRQL) or patient reported outcomes (PRO) data. Furthermore, the CDF requires data collection over 24 months, which is often insufficient time to develop and extract data from a de novo registry, particularly using paper-based data capture.

The value of patient reported outcomes

Treatment is becoming increasingly patient-centred; regulators, HTA agencies and other healthcare decision-makers are increasingly interested in patients' experience of living with a condition and being treated for it, using measures which ask the patient directly.

PRO data, including HRQL, symptoms and daily functioning, are becoming increasingly important to provide an overall view of the burden of a disease and context to the potential value of treatment.

In many instances, PROs provide the most accurate and precise description of disease burden and the impact of treatment.

PROs are typically measured using instruments that have been developed for this purpose. These include disease-specific instruments designed to be used to measure outcomes in a specific indication such as the EORTC QLQ-C30, a measure of quality of life in cancer patients.

Whilst PROs are increasingly evaluated in clinical trials in some disease areas, they are considered less often in the real-world setting. Collection of PROs in the real-world has significant additional value compared with PROs measured within clinical trials. The data:

- are collected in "real-time"
- include different cohorts of patients, with co-morbidities that are not included in RCTs
- provide increased opportunity for patients to report symptoms difficult to capture on trial visits, such as daily burden of disease, diet and exercise
- demonstrate how a condition such as melanoma and its treatments affects patients in the long term.

The MyRealWorld™ melanoma registry

The Melanoma Registry has been developed in collaboration with the Patient Advocacy Organisation (PAO) Melanoma UK and the Royal Marsden NHS Foundation Trust (London).

The Registry records patient demographics, treatment patterns, AEs, ECOG performance status, diet and exercise, as well as monthly PRO data:

Patients complete EQ-5D-5L, EORTC QLQ-C30 and a melanoma-focused subset of the PRO-CTCAE using the study app on their mobile devices ("bring your own device" [BYOD] technology).

Development of the app was informed by feedback from patients and Melanoma UK.

Patients with any type or stage of melanoma are recruited in collaboration with Melanoma UK.

The registry was launched at the end of October 2017.

Ethics approval has been obtained.

Informed consent is obtained electronically via the study app.

The study is fully GDPR compliant.

The study protocol has been registered with clinicaltrials.gov:

- ID NCT03379454
- Study title: The impact of melanoma and drug treatment in the real-world

RIGOUR	SPEED	GRANULARITY	CO-CREATION
Ethics approval GDPR/HIPAA SABs ISO certification Valid PRO instruments	Community-based recruitment Close to real-time data access Built-in stats	International Any language Not just clinic visits	Patient advocacy partnerships Gamification

Patient recruitment & inclusion criteria

Patients are recruited in collaboration with the Melanoma UK.

The patient inclusion criteria are broad to ensure that a wide selection of people is recruited:

- resident in UK; with NHS (or CHI) number
- current or previous diagnosis of melanoma
- age ≥18 years
- willing to use their own smartphone or tablet.

Study objective

The aim of the present study was to conduct an analysis of the EQ-5D-5L data recorded in the registry in order to :

- compare EQ-5D-5L utility values in patients with melanoma in the real-world setting collected using a digital real-world evidence app versus literature values
- identify key determinants of utility

METHODS

Our methodology consisted of two steps:

- Analysis of the EQ-5D-5L data collected through the app
  - Utilities were calculated using the EuroQol UK algorithm
- Scoping literature search on PubMed, to understand the published data on real-world utilities.

The EQ-5D-5L

The app includes the UK version of the EQ-5D-5L instrument, comprising 2 elements:

- the EQ-5D descriptive system
- and the EQ visual analogue scale (EQ VAS)

The EQ-5D-5L descriptive system comprises the following 5 dimensions:

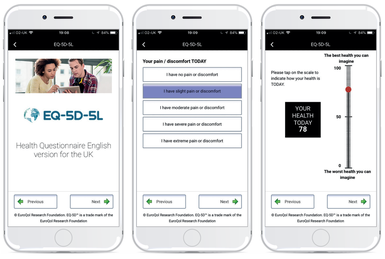
mobility, self-care, usual activities, pain/discomfort and anxiety/depression

Each dimension has 5 levels:

no problems, slight problems, moderate problems, severe problems, and extreme problems.

The respondent is asked to indicate his/her health state by selecting the most appropriate statement in each of the 5 dimensions.

The EQ VAS records the respondent's self-rated health on a vertical, visual analogue scale where the endpoints are labelled 'The best health you can imagine' and 'The worst health you can imagine'. This information can be used as a quantitative measure of health outcome as judged by the individual respondents.



RESULTS

Note: The results presented here are based on 88 registry participants who provided EQ-5D-5L and disease stage data from a total sample of 145 participants recruited at the time of the data cut.

309 participants are currently registered

Patient demographics

Figure 1: Patient sample by stage

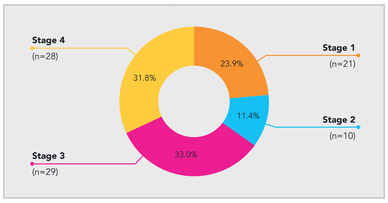
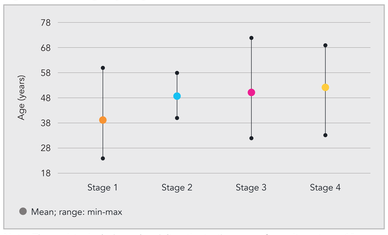
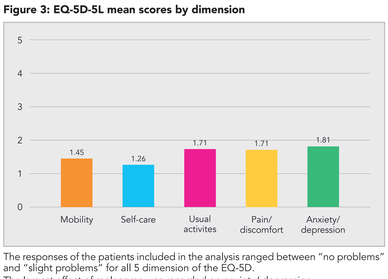


Figure 2: Mean age by stage



Note: The registry includes only adult patients, thus age of recruitment was 18

Figure 3: EQ-5D-5L mean scores by dimension



The responses of the patients included in the analysis ranged between "no problems" and "slight problems" for all 5 dimension of the EQ-5D.
The largest effect of melanoma was recorded on anxiety/ depression

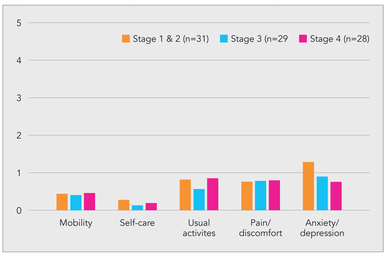
Table 1: Numbers and proportions of patients reporting levels within EQ-5D dimensions by stage

	Mobility		Self-care		Usual activities		Pain/ discomfort		Anxiety/ depression	
Level	Stage 1/2 (n=30)	Stage 3/4 (n=57)	Stage 1/2 (n=30)	Stage 3/4 (n=57)	Stage 1/2 (n=30)	Stage 3/4 (n=57)	Stage 1/2 (n=30)	Stage 3/4 (n=57)	Stage 1/2 (n=30)	Stage 3/4 (n=57)
1	80.0%	77.2%	83.3%	89.5%	60.0%	61.4%	53.3%	50.9%	30.0%	43.9%
2	16.7%	12.3%	10.0%	8.8%	23.3%	26.3%	33.3%	35.1%	50.0%	45.6%
3	0%	10.5%	6.7%	1.8%	6.7%	8.8%	10.0%	14.0%	13.3%	10.5%
4	0%	0%	0%	0%	3.3%	1.8%	3.3%	0%	3.3%	0%
5	3.3%	0%	0%	0%	6.7%	1.8%	0%	0%	3.3%	0%
Some problems	20.0%	22.8%	16.7%	10.5%	40.0%	38.6%	46.7%	49.1%	70.0%	56.1%

Level 1: indicating no problem. Level 2: indicating slight problems. Level 3: indicating moderate problems. Level 4: indicating severe problems. Level 5: indicating extreme problems.

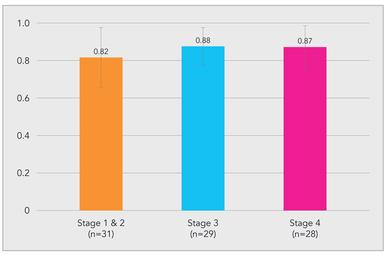
For all dimensions except for anxiety/depression participants are more likely to report no problems than some problems (Table 1). Anxiety/depression is a problem for 70% of stage 1/2 participants and this is perhaps due to the fact that these patients might have been recently diagnosed with the disease. About half of participants report some problems with pain/discomfort for both groups and about half of stage 3/4 report some problems for anxiety/depression. Very few participants report moderate or higher problems on any of the five domains for any stage.

Figure 4: Mean scores by dimension and disease stage



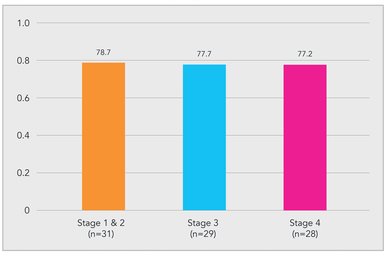
Anxiety/ depression is affected most at the earlier stages of the disease, when diagnosis is more recent. (Figure 4) The responses ranged between "no problems" and "slight problems" for all 5 dimension of the EQ-5D and across all disease stages.

Figure 5: Mean utility score by stage



Stage 1/2 patients have reported slightly lower mean utility score than stage 3 and 4 patients (Figure 5), which could be driven by the increased anxiety/depression scores reported in the early stages of the disease.

Figure 6: Mean EQ VAS score by stage



Overall, patients' self-rated health does not change across disease stages (Figure 6).

Results of the scoping literature search

Overall, there is a limited number of studies which have estimated EQ-5D derived utilities for melanoma[6–9].

No studies collecting EQ-5D data for melanoma outside the clinical setting were identified:

- The study by Dixon *et al.* (2006)[10] used the EQ-5D-3L questionnaire within an RCT to estimate utilities of stage 3 melanoma patients randomized to either interferon alpha-2a or placebo.
- The EQ-5D-5L questionnaire was used in the study by Tromme *et al.*[9]; however, patients were recruited within the clinic and not in the real-world setting.

Use of RWE in melanoma HTAs

In addition, very limited use of real-world HRQL data in HTAs and relative effectiveness assessments (REAs) has been identified.

The Makady *et al.* (2018) study examined the extent to which real-world data was included in HTA reports of seven melanoma drugs from five different agencies[11]. Of the 52 reports identified, only 4 included real-world HRQL data, one of which came from a registry.

DISCUSSION

To the best of our knowledge, there are very limited studies with the use of EQ-5D-5L in melanoma patients, none of which were conducted in the real-world setting.

The present study is an early analysis of the melanoma registry baseline data only.

The full registry includes longitudinal EQ-5D utility data recorded within the real-world setting, making them available in real time.

This, in combination with the fact that the BYOD app provides benefits in terms of the frequency of data recording (patients opted to complete surveys more frequently than the suggested monthly) and completion rates, gives the opportunity of a unique and granular dataset.

CONCLUSIONS

As melanoma treatment continues to evolve, utility values recorded in the real-world setting in close to real-time will offer important insights to drug developers, HTA agencies, clinicians and patients.

The richness of the information in the digital registry will enable exploration of the impact of a wide range of parameters in the real-world setting that are not well documented in literature.

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