Progressi nel monitoraggio della qualità della vita dopo il trattamento oncologico
«Ruolo della tecnologia *in tasca al paziente*»
Parma, 19/03/2024

BD4QoL: uno studio multicentrico randomizzato per il monitoraggio della qualità della vita nei pazienti curati per tumori del distretto testa-collo, basato su nuove tecnologie

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DI MILANO

Conflitti di interesse

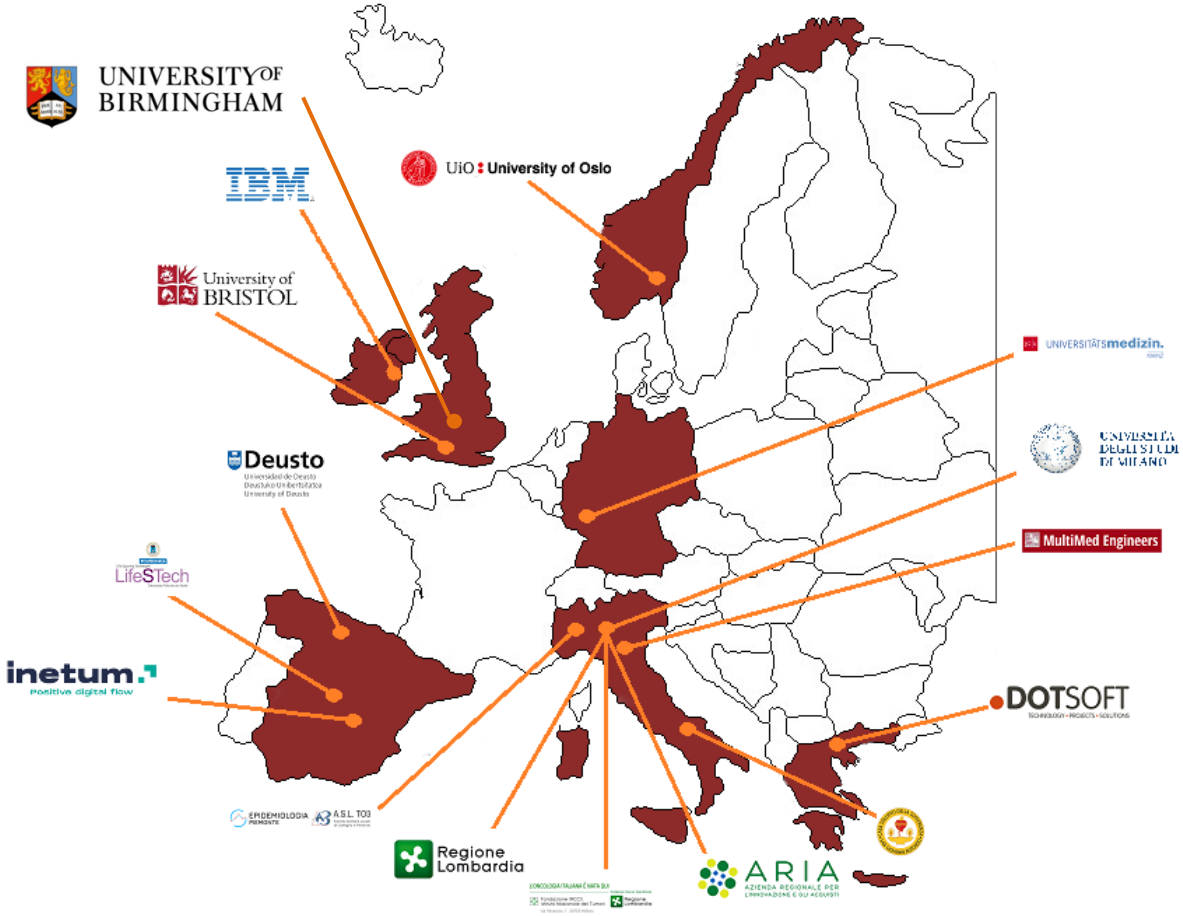
- Accademia Nazionale di Medicina

Big Data Models and Intelligent tools for Quality of Life monitoring and participatory empowerment of head and neck cancer survivors

BD4QoL

http://www.bd4qol.eu/

BD4QoL Project Consortium

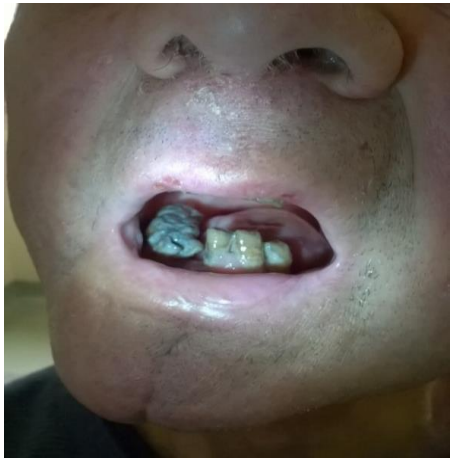


BD4QoL
BIG DATA FOR QUALITY OF LIFE

Background – head and neck cancer

- >90% squamous cell carcinomas (HNSCC)
- Risk factors: smoking, alcohol, HPV
- Stage
  - 1/3 early (I/II) → 80-90% cured
  - 2/3 loco-regionally advanced (III/IV) → up to 50% relapse within 2 years
- Quality of life (QoL) issues: global QoL recovery by 12 months after treatment, BUT a quota of persistent late sequelae are observed, notably deterioration in physical functioning, fatigue, xerostomia and sticky saliva

Cancer recurrence



Oral cavity unresectable oral recurrence (+trismus)

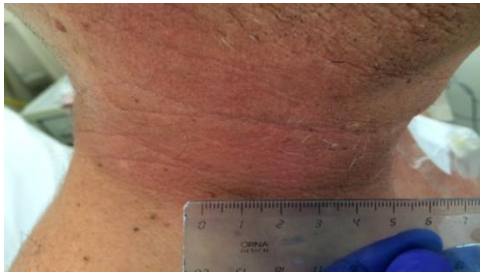
Oropharyngeal recurrence (+trismus) not amenable to salvage RT

Regional recurrence not amenable to local therapies

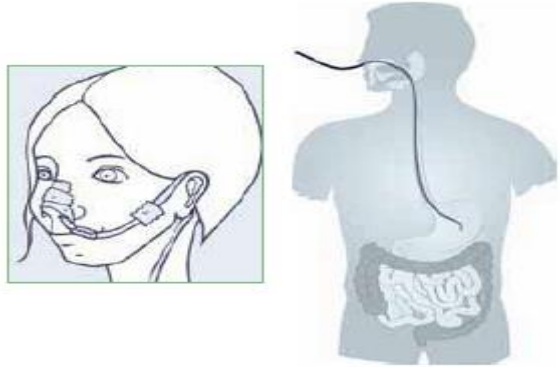
Skin HNC local recurrence

Acute treatment toxicities

Mucositis



Radiodermitis



Nasogastric feeding tube

Late sequelae in HNC survivors

Neck edema and fibrosis

Gastrostomy

Tracheostomy

Fistula

Osteonecrosis

Background – QoL questionnaires

- 3 main validated questionnaires available
  - EORTC QLQ-C30 for all types of malignancies
  - EORTC HN43 for HNC patients only
  - EQ-5D-5L which is a patient-reported measurement used for health technology assessment (HTA)
- In some subset like NPC, QoL alterations are associated with OS
- Replicable methods to minimize misinterpretation and to maximize the accuracy in measuring QoL variations
  - E.g., overall indicator such as global health status according to EORTC QLQ-C30* a deterioration is considered clinically meaningful in case of a score reduction of at least 10 points**
- Current standard: repeated QoL questionnaires

References:

** Aaronson 1993*

*** Osoba 1998, Cocks 2012*

Physical activity

EORTC QLQ-C30

1. Do you have any trouble doing **strenuous activities**, like carrying a heavy shopping bag or a suitcase?
2. Do you have any trouble **taking a long walk**?
3. Do you have any trouble **taking a short walk** outside of the house?
4. Do you need to **stay in bed or a chair** during the day?
6. Were you limited in doing either your work or other daily activities?
8. Were you **short of breath**?
10. Did you need to **rest**?
18. Were you **tired**?

Sleeping

EORTC QLQ-C30

10. Did you need to **rest**?
11. Have you had trouble **sleeping**?
12. Have you felt weak?
18. Were you tired?
20. Have you had difficulty in concentrating on things, like reading a newspaper or watching television?

Social activity

EORTC QLQ-C30

5. Do you need help with eating, dressing, washing yourself or using the toilet?
6. Were you limited in doing either **your work or other daily activities**?
7. Were you limited in pursuing **your hobbies or other leisure time activities**?
12. Have you felt weak?
13. Have you lacked appetite?
14. Have you felt nauseated?
15. Have you vomited?
16. Have you been constipated?
17. Have you had diarrhea?
18. Were you tired?
19. Did pain interfere with your daily activities?
20. Have you had difficulty in **concentrating on things, like reading a newspaper or watching television**?
21. Did you feel tense?
22. Did you worry?
23. Did you feel irritable?
24. Did you feel depressed?
25. Have you had difficulty remembering things?
26. Has your physical condition or medical treatment interfered with your **family life**?
27. Has your physical condition or medical treatment interfered with your **social activities**?
28. Has your physical condition or medical treatment caused you **financial difficulties**?

QoL-related «behavioral features»

- Physical activity
- Sleeping
- Social activity

Emerging needs

- **Survivors** feel alone, without clear and constant reference, and exhibit highly individualized approaches to self-management
- **GPs and welfare services** are not fully included into HNC post-treatment management nor have direct and coordinated links with the specialists engaged in survivors' follow-up at the cancer center
- **Point-of-care physicians** have limited insight on patients' perceptions of QoL, since, at present, QoL and PROMs monitoring it is not included in the standard of care. Extra workload and effort would be required. Dedicated resources need to be allocated.
  - **BUT: QoL monitoring and self/management has shown significant impacts on patients wellbeing and survival**

- **BD4QoL challenges new unobtrusive systems and approaches (mHealth AI algorithms, chatbots and emerging mobile technologies familiarity among all strata of population**)

Clinicians' vision: concept & objectives

By

- Unobtrusively collecting behavior data that are known to be correlated to QoL items (physical activity, sleeping, social activity)
- Empowering and supporting patients (chatbot) with personalized contents
- Real-time and timely informing clinicians (alerts, point-of-care dashboard)

We will

- Identify QoL correlates and their alterations during follow-up
- Identify predictive models of disease outcome
  - Local, loco-regional, distant, 2nd primary T
- Identify prognostic models
- Integrate knowledge from historical datasets and randomized controlled trial

Aiming at

- Preventing QoL deterioration in HNC survivors over standard care
- Generating a large dataset (ensuring data diversity) for future research

BD4QoL solution

- Leverage mobile technologies and mobile apps (e.g. Google Fit) already in use by survivors for unobtrusive data collection (real-life setting, survivor's own smartphone)
- Benefit from data already collected by smartphone sensors to derive QoL indicators
- Use advanced algorithms for the delineation of survivor behaviors correlated with QoL
- Provide real-time support (on demand) and lifestyle behavior improvement motivation
- Facilitate PoC monitoring through smart alerts and patient status dashboard
- Apply AI to model QoL trajectories, early identify QoL deterioration and classify patients by risk of QoL decrease and poor outcome

- At the same time preserving patient's privacy and rights regarding their health status management

BD4QoL - Historical study

Database /	Providing institution	No. of patients	Stage	Clinical data #	Pathology (*) biomarkers/Staging	Risk factors	Treatment (°)	Biological samples	omics origin of sample (T,G) &	QoL data	QoL data timing	QoL questionnaires used	Mean follow-up (mo.)	Ethics Approval for future studies
INT-BD2D-R	INT	305	III-IVa-b	yes	yes	yes	yes	305	tumor FFPE (T+G)	No	No	No	46 mo.	yes
INT-BD2D-P		195	III-IVa-b	yes	yes	yes	yes	195	tumor FFPE (T+G)	Yes	baseline, 6, 12 mo.	HN30-HN35-EQ5	24 mo.	yes
Ongoing	CSS	100	I-IV	yes	(80)	yes	yes	90	formalin fixed blocks	N/A	N/A	N/A	N/A	yes (90 pts)
Ongoing		80	I-IV	yes		yes	yes	80	formalin fixed blocks	N/A	N/A	N/A	N/A	yes
UMM 01	Mainz	218	I-IV	yes	no	yes	partly	no	n.a.	Yes	cross-sectional	C30, HN35	80 mo	only for this study, to be collected
UMM 02		300	I-IV	yes	no	yes	partly	no	n.a.	Yes	before surgery, after surgery, 6m, 12m, 24m, 36m	C30, HN35	36 mo	only for this study, to be reconfirmed
UMM 03		246	I-IV	yes	no	yes	partly	no	n.a.	Yes	cross-sectional	C30, HN35	59 mo	only for this study, to be reconfirmed
UMM 04		300	I-IV	yes	no	yes	partly	no	n.a.	Yes	before surgery, after surgery, 6m, 12m	C30, HN35	12 mo	only for this study, to be reconfirmed
UMM 05		113	I-IV	yes	no	yes	partly	no	n.a.	Yes	admission to hospital, discharge, 12m	C30, HN35	12 mo	only for this study, to be reconfirmed
UMM 06		677	I-IV	yes	no	no	yes	no	n.a.	Yes	before TX, 3m, 6m	C30, HN43	6 mo	yes
UMM 06		135	I-IV	yes	no	no	yes	no	n.a.	Yes	cross-sectional (min 24m after diagnosis)	C30, HN43	60 mo	yes
Head and neck 5000	Bristol	5511 (§)	I-IV	yes	yes	yes	partly	yes	formalin fixed blocks	yes	pre- treatment, 4mo, 12mo, 3yr+	EQ5, Bristol questionnaires	>48 mo	yes
TOTAL §		8.180												

Note: # needed minimum information: sex, age, stage, localization
° needed information: type, drug, timing, dose
§ Data from Bristol must be selected to exclude cancer not included in BD4QoL study (expected 20% drop-outs)
* needed information: histology, HPV status (p16 or HPV-DNA)
& T: gene expression; G: mutational status

BD4QoL
BIG DATA FOR QUALITY OF LIFE

Benchmark for sample size calculation

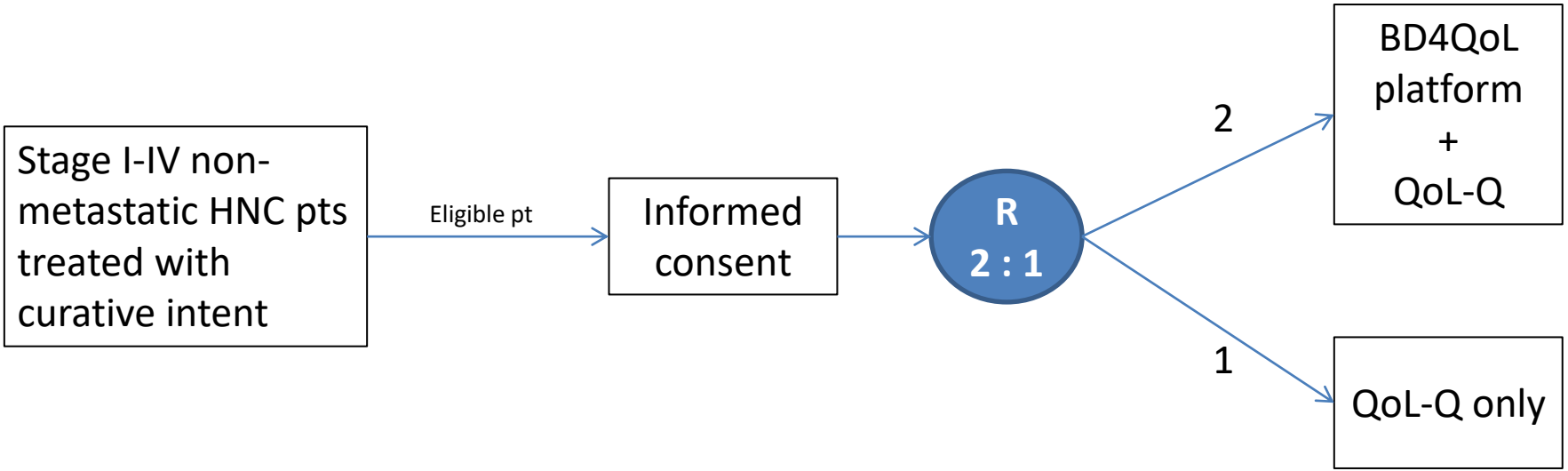
Retrospective dataset	Nr. cases	% of HNC survivors with a clinically meaningful deterioration of overall QoL (global health status)
BD2Decide	117	19%
Mainz	65	23%
HN5000	1241	18%

Average = 20%

- **H_0**: % of clinically meaningful deterioration in BD4QoL **without tools** =
= % of clinically meaningful deterioration in retrospective data → **20%**

- **H_1**: % of clinically meaningful deterioration in BD4QoL **with tools** =
= **-10%** of clinically meaningful deterioration in retrospective data → **10%**

Study design



Sample size (including 20% dropout):
140 control group + **280** intervention = **420**

Primary objective and endpoint

Objective	***Endpoint***
↓ % of HNC subjects experiencing a clinically meaningful deterioration of QoL between at least 2 visits during post-treatment fup	The proportion of HNC survivors experiencing a clinically meaningful global health related EORTC QLQ-C30 QoL deterioration (decrease ≥10 points*) within the study observation (up to 24 months) period during post-treatment follow-up.

** References: Osoba, JCO 1998; Cocks, EJC 2012*

Secondary objectives and endpoints

Objective	***Endpoint***
To delay the time to the first clinically meaningful deterioration of QoL between at least 2 visits during post-treatment fup	The time-to-first clinically relevant deterioration of EORTC QLQ-C30 global score
↓ % of HNC subjects experiencing a clinically meaningful deterioration in EORTC QLQ-C30 scales	EORTC QLQ-C30 scales: emotional functioning, role functioning, fatigue
↓ % of HNC subjects experiencing a clinically meaningful deterioration in EORTC QLQ-HN43 scales	EORTC QLQ-HN43 scales: swallowing, problems with teeth, problems opening mouth, speech, social eating, fear of progression
↓ % of HNC subjects of HNC subjects experiencing a clinically meaningful deterioration in EQ-5D-5L domains	EQ-5D-5L domains: mobility, self-care, usual activities, pain/discomfort, anxiety/depression

Prospective protocol – RCT flowchart

Procedure/evaluation	Study entry	Continuous (for up to 24 months from study entry)	Months +6, +12, +18, +24 (±2 weeks)
Informed consent	X		
Baseline evaluation: demographics, clinical data (stage, pathology, HPV) and treatment data	X		
Clinical data collection	X		X
Concomitant medications and medical events review	X		X
Physical/emotional/social monitoring apps	X	X	X
QoL data	X		X

Intervention = the BD4QoL platform

- Mobile App
  - including the chatbot
- PoC dashboard
- RedCAP (eCRF)
- QoL questionnaire tool

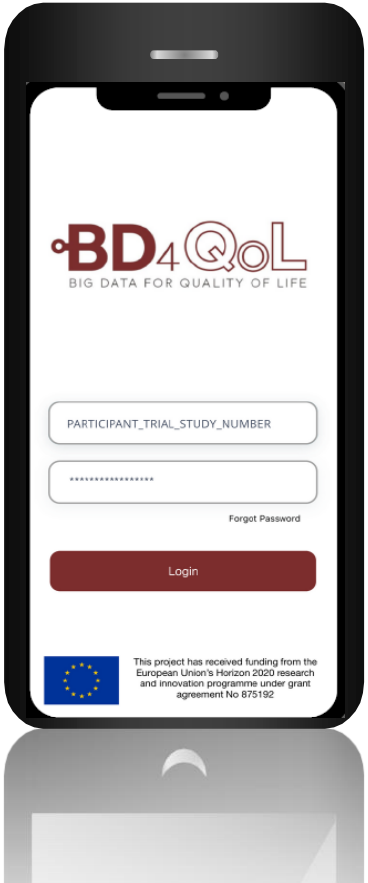
BD4QoL Mobile App (Android)

•Android smartphones are used as the personal smartphone devices for data collection, in order to enable big data phone (social) data collection (iOS blocks any API requests for related data)

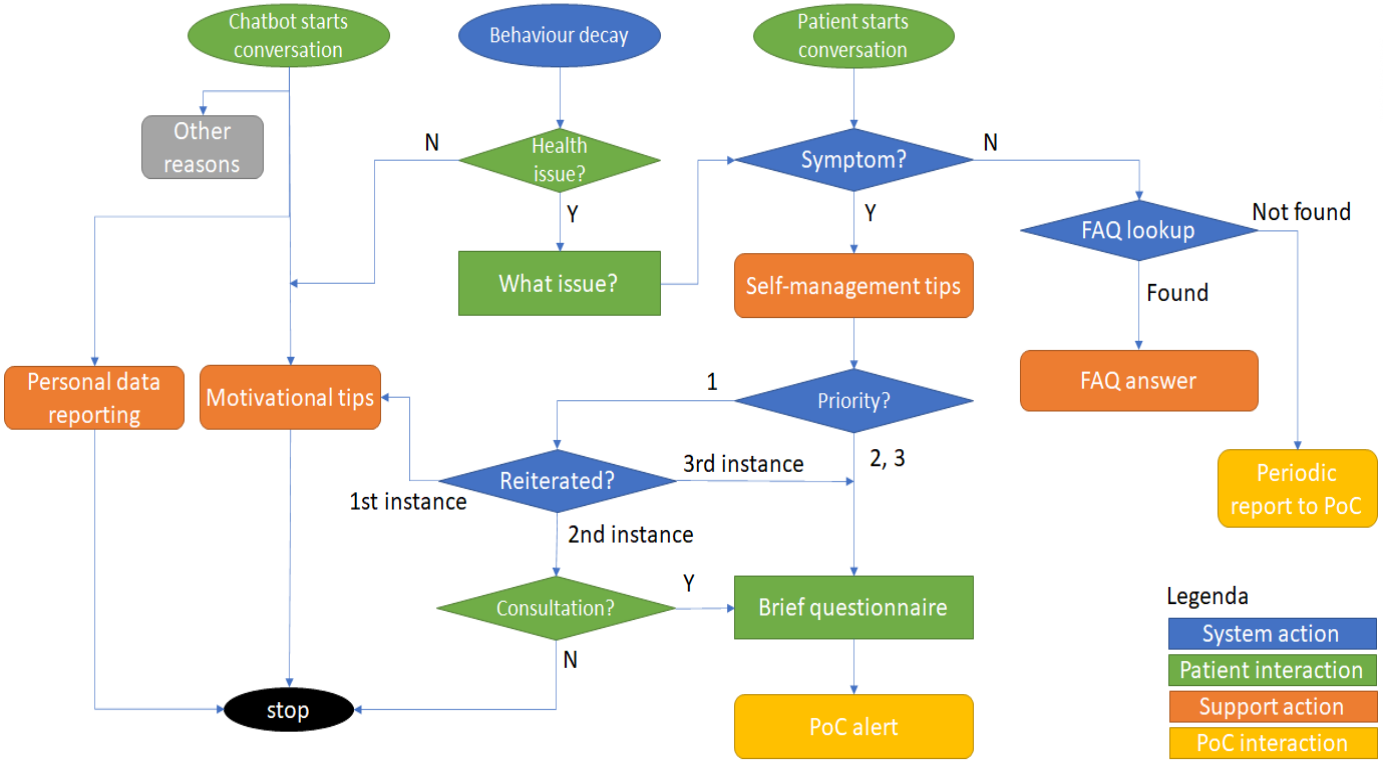
Google Fit is used as an external dataset for physical data collection (STEPS)

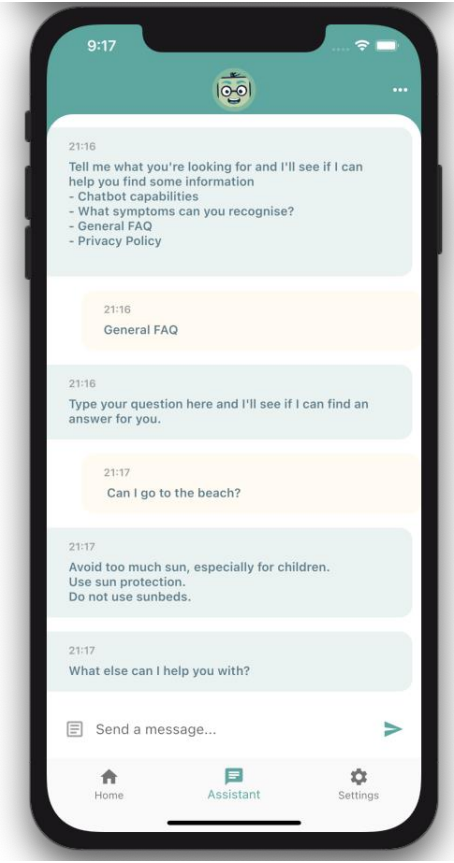
1 Foreground mobile application

GPS, LIGHT, SCREEN, Activity Recognition, Accelerometer, WiFi



BiDi: the BD4QoL chatbot

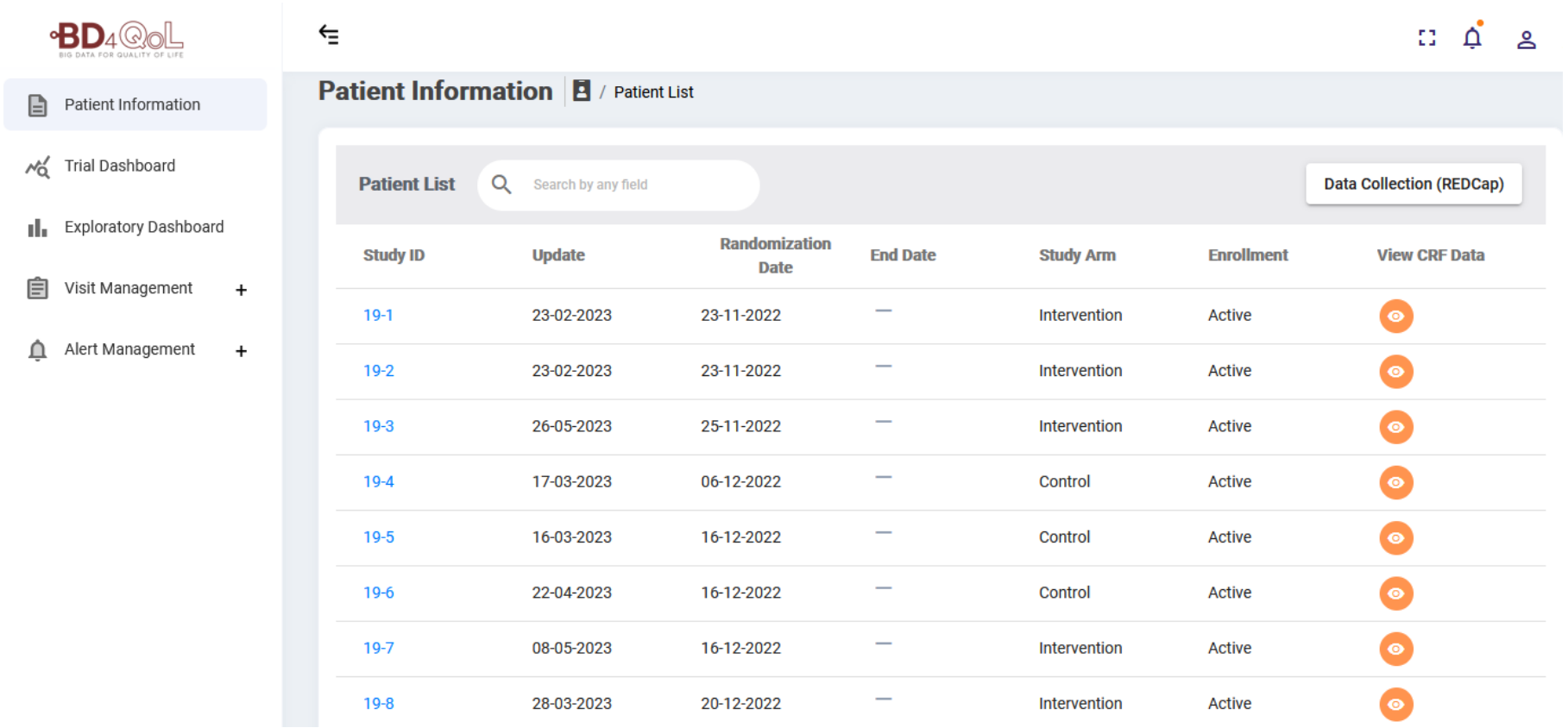


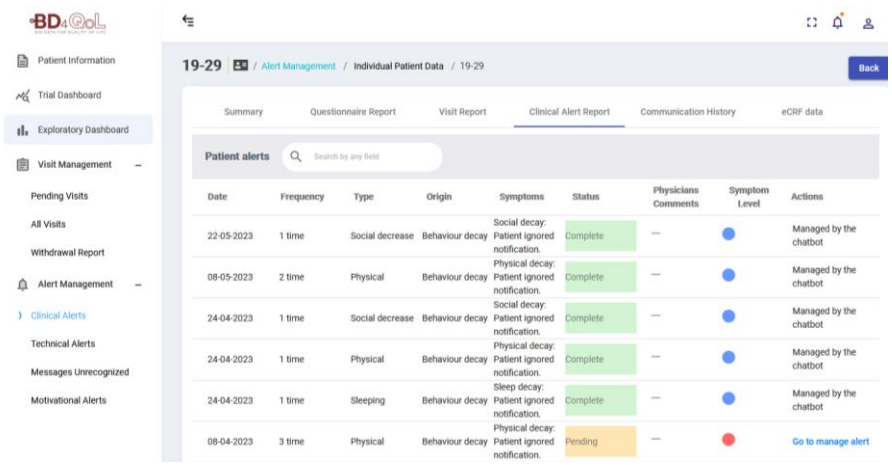


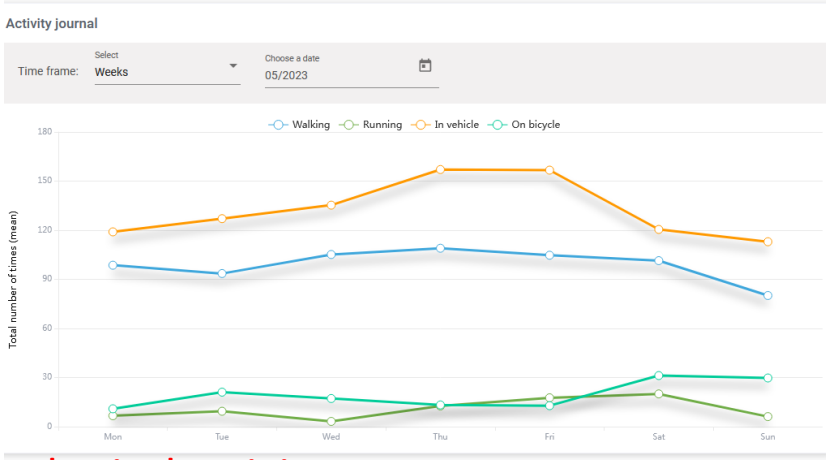
Possible “user-BiDi” utterance

Adverse Event	User examples	Tips and recommendations
Dry mouth	I’m feel thirsty all the time Feels like my mouth is really dry I need to drink often I have xerostomia I wake in night with a dry mouth I have no/less saliva My mouth is arid	Treatments for head and neck cancer often affect saliva production But a dry mouth can also be caused by dehydration , or eating lots of salty foods. Some medication can also cause your mouth to feel dry ● Keep a bottle of water with you and sip regularly ● If you feel thirsty it may be that you are not drinking enough fluids. Aim for 6 – 8 glasses of fluid each day (only if there is no medical contraindication). ● Try using chewing gum to increase saliva. ● If you are already drinking plenty of fluid and you still feel thirsty please contact your doctor You may want to try some products that are available from online shopping websites. These products will not cure your dry mouth, but some people who have received similar treatments to yours have found them helpful.

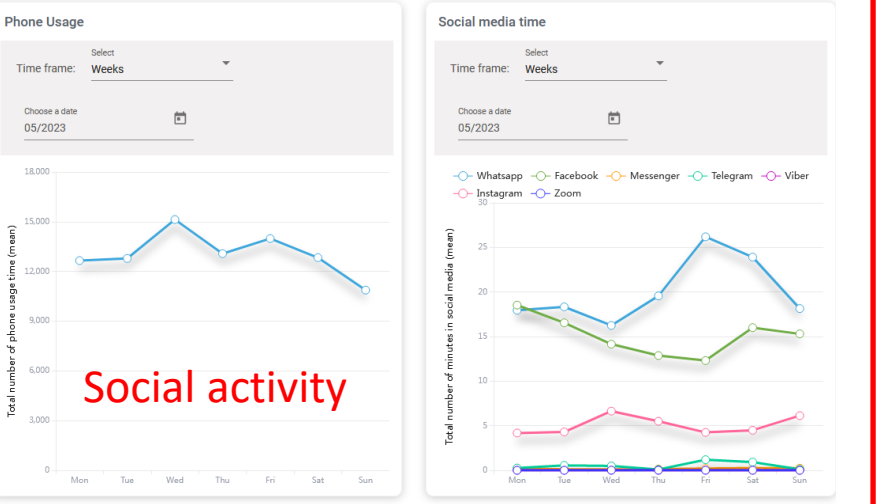
BD4QoL PoC dashboard



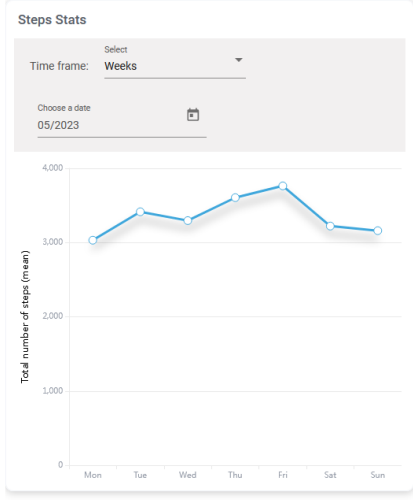


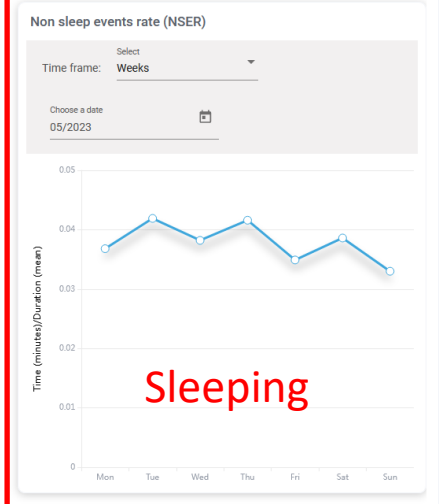


Physical activity



Social activity





Sleeping

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A multicenter randomized trial for quality of life evaluation by non-invasive intelligent tools during post-curative treatment follow-up for head and neck cancer: Clinical study protocol

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