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Single Day Event

Real-World Evidence (RWE) for Oncology Drug Development

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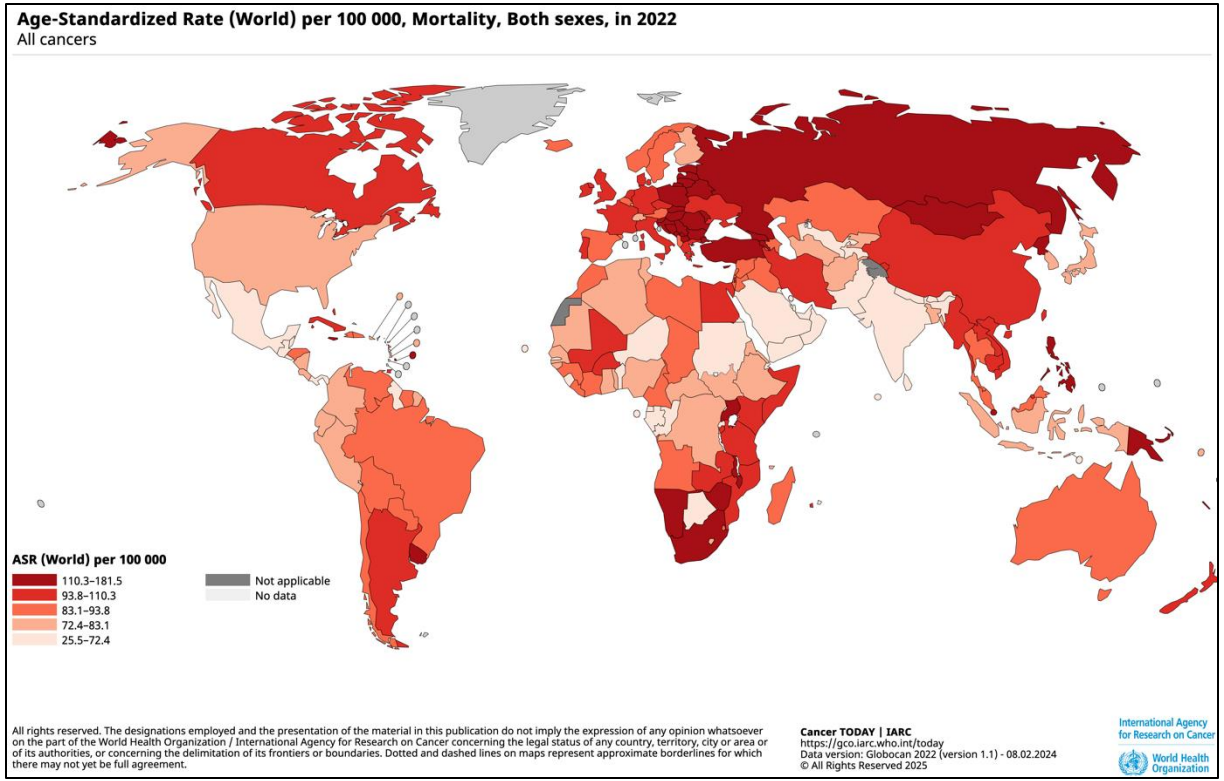
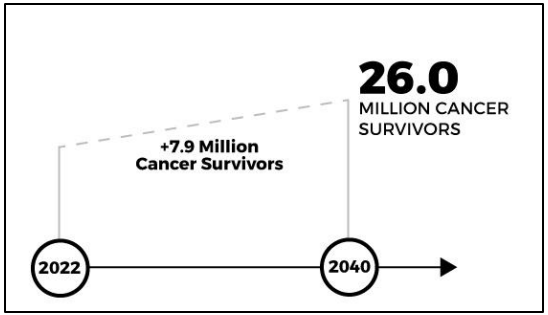
Navitas Life Sciences, Bangalore

Phuse SDE, 22 March 2025, Pune

Cancer – leading or second leading cause of death in 112 of 183 countries



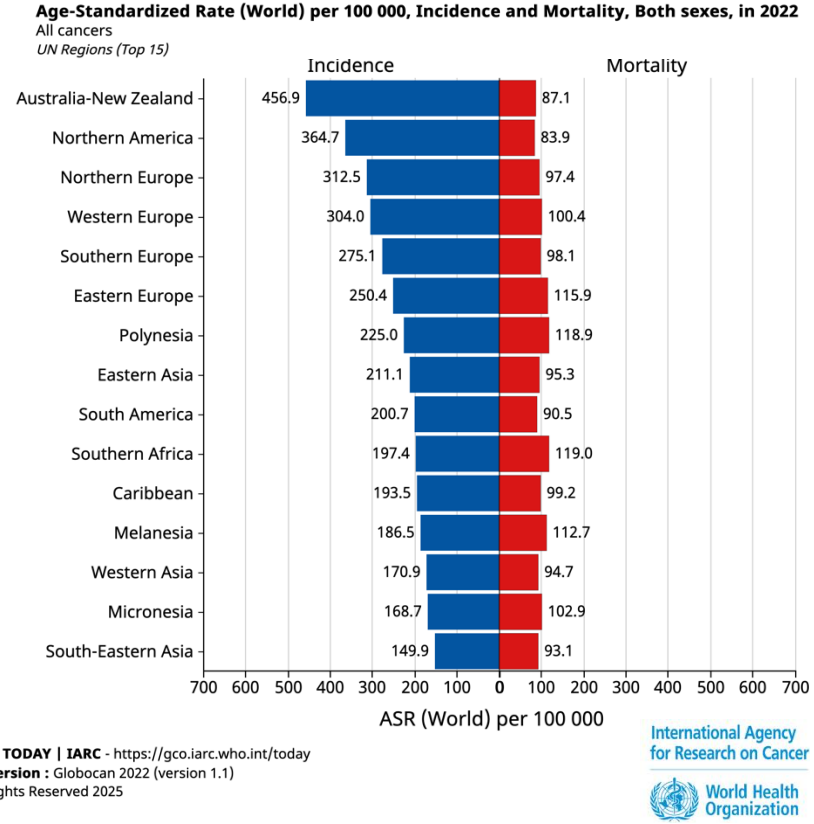
Year 2022

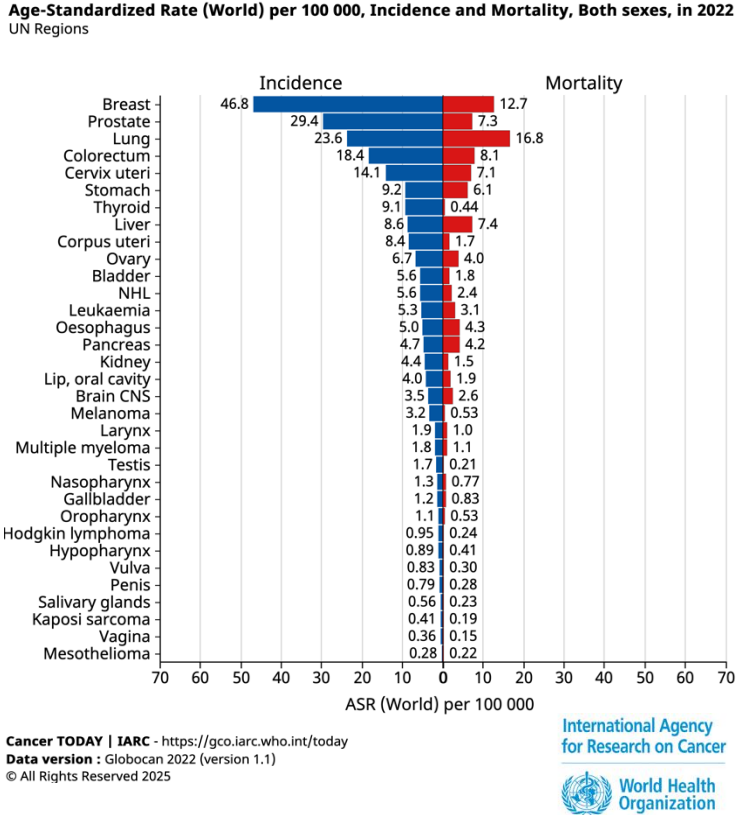


https://cancercontrol.cancer.gov/ocs/statistics

Gallicchio L *et. al* (2022) JCNI

Cancer type and access to care influence mortality and incidence rates





Drug development can cost $1 - $2.6 billion and 10-18 years

Cancer drug approval rate - < 5 %

DiMasi, J. A., Grabowski, H. G., & Hansen, R. W. (2016)
The Cost of Developing a New Drug, Tufts Center for the Study of Drug Development.
U.S. Food and Drug Administration (FDA) (2022). FDA's Drug Approval Process.

How can Real-World Data and Real-World evidence help?

What is Real-World Data (RWD) and Real-World Evidence (RWE) ?

FDA definition…

Real-world data (RWD) are data relating to patient health status and/or the delivery of health care routinely collected from a variety of sources.


Electronic Health Records (EHR)


Pharmacy and Prescription Data


Lab and Diagnostic Data

Insurance claims


Health Surveys and population studies

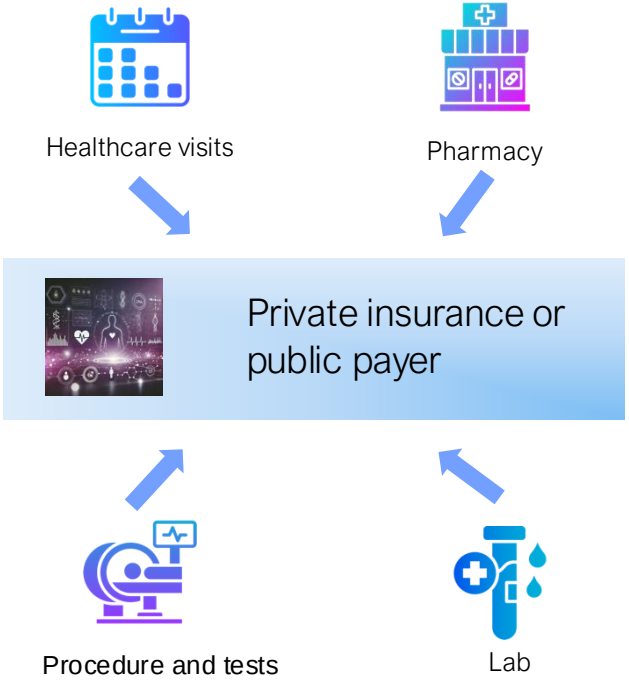

Genomic and Biomarker Data


Patient registry


Wearable Devices and Sensors


Public Health Databases

RWD is collected during routine health-care delivery



Example Real-World database

Adapted from National Health Council Webinar - Real-World Data and Real-World Evidence 101 (link)

Real-World evidence is generated using Real-World data

Real-world evidence is the clinical evidence about the usage and potential benefits or risks of a medical product derived from analysis of RWD.

RWD Sources

- Electronic Health Records (EHR)
- Insurance claims
- Patient registry
- Pharmacy and Prescription Data
- Health Surveys and population studies
- Wearable Devices and Sensors
- Lab and Diagnostic Data
- Genomic and Biomarker Data
- Public Health Databases

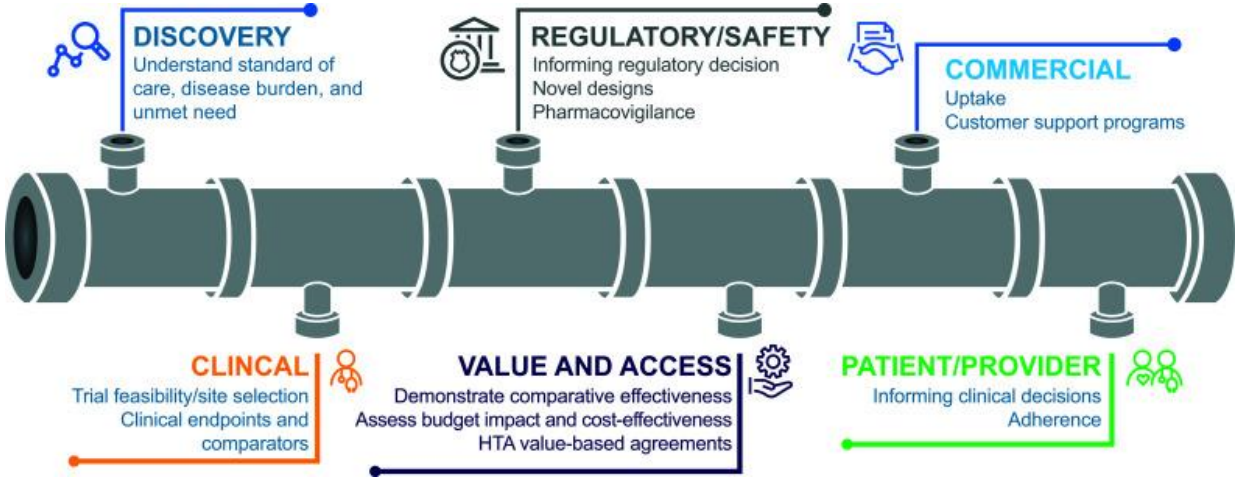
Real-World data

Analyzed as per research objectives

Real-World evidence

Adapted from National Health Council Webinar - Real-World Data and Real-World Evidence 101 (link)

Uses for RWD throughout the drug development pipeline



1. **Enhancing Clinical Trial Design and Population Representativeness**
2. **Post-Marketing Surveillance and Safety Monitoring**
3. **Advancing Personalized Medicine in Oncology**
4. **The future of RWE in Oncology**

Image reference - Yap TA, Jacobs I, Baumfeld Andre E, Lee LJ, Beaupre D, Azoulay L. Application of Real-World Data to External Control Groups in Oncology Clinical Trial Drug Development. Front Oncol. 2022 Jan 6;11:695936. doi: 10.3389/fonc.2021.695936. PMID: 35070951; PMCID: PMC8771908.

1. Enhancing Clinical Trial Design and Population Representativeness

Clinical Trial

Selective study population

Exclusion -

- >75 Age
- Comorbidities
- Prior malignancy, diabetes, kidney, liver diseases

Result – 30 - 40 % patients ineligible for trials.
~ 3 % patients in breast cancer clinical trial.

RWD

Broader population inclusion

Inclusion –

- Elderly patients with multiple heath conditions.
- Ethnic minorities.

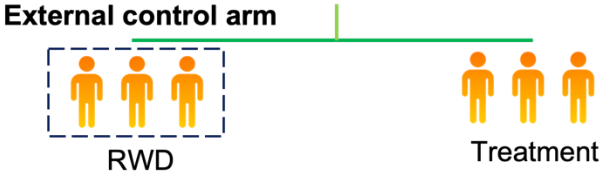
Result – Complement findings of RCT in patients not eligible for clinical trial (Trial Pathfinder framework)

Rare cancer or less common subgroups

Clinical trial infeasible or unethical

External control arm

RWE to support regulatory decision making in smaller sub-groups



Merkel cell carcinoma

BAVENCIO® avelumab Injection 20 mg/mL

EMD SERONO

Pfizer

- Accelerated approval by FDA (2017) for metastatic Merkel cell carcinoma and urothelial carcinoma.
- Single-arm, open-label, Phase II study, JAVELIN Merkel 200.
- RWD confirmed effectiveness (ORR) & durability in the absence of an RCT.
- Full approval in 2020 using external controls.

Acute lymphoblastic leukemia

BLINCYTO® (blinatumomab) for injection 35 mcg single-dose vial

AMGEN®

- Accelerated approval by the FDA (2014) and EMA (2015) for R/R Philadelphia chromosome-negative ALL
- RWE validated OS benefit and supported full FDA Approval (2017).
- Real-world data informed FDA's decision to approve MRD+ indication (2018).
- RWD/RWE confirmed safety in older & high-risk patients for broader clinical use.

Male breast cancer

IBRANCE® palbociclib 125 mg capsules

Pfizer

- HR+/HER2- advanced/metastatic breast cancer (FDA, 2015)
- Label expansion in males based on on post-marketing reports and electronic health records.
- Safety profile in males similar to consistent with tolerability with females.

2. Post-Marketing Surveillance and Safety Monitoring

Rare or delayed adverse events

RCT

- Limited sample size
  (Low incidence AE ~ 1 in 10000)

- Short Follow-Up durations

- Homogenous study populations

Drug / Therapy	Cancer	Risk/Incidence	Data source
Trastuzumab ± Pertuzumab	HER2-positive breast cancer	Left ventricular dysfunction and heart failure[1,2]	Claims and registry data
Immune checkpoint inhibitors (ICI)	Adv. Melanoma NSCLC, RCC, Hodgkin lymphoma	Secondary Malignancy[3,4] Hematalogic or Solid tumors	EHR from multiple centers
CAR T-cell therapy	Relapsed/Refractory B-Cell Lymphomas	Cytokine release syndrome (CRS) Immune effector cell-associated neurotoxicity syndrome (ICANS)[5]	Registry data

1. Pivot X et al. Cardiac safety of trastuzumab in the real-world setting: final results of the French observational study. BMC Cancer. 2015;15:1012.
2. Long-Term Cardiotoxicity of HER2-Targeted Therapy in Early-Stage Breast Cancer: A 10-Year Follow-Up Study Using Real-World Data." Breast Cancer Res Treat. 2021;188(1):175-184.
3. Johnson DB, Sullivan RJ, Menzies AM, et al. "Long-term outcomes and secondary malignancies in advanced melanoma patients receiving combination ipilimumab and nivolumab: A multicenter real-world study." Oncologist. 2022;27(6):e541-e550.
4. Shen X, Zhuang W, Yang Z, et al. "Risk of secondary primary malignancies following immunotherapy: A nationwide real-world analysis." Cancer Med. 2022;11(24):4896-4904.
5. Roberts ZJ, Diaz AJ, Fu B, et al. CAR T-Cell Therapy–Associated Neurotoxicity and Cytokine Release Syndrome in a US Real-World Cohort of Patients with Relapsed/Refractory B-Cell Lymphomas." Blood Adv. 2023;7(2):388-397.

RWE and surveillance systems facilitates the continuous monitoring and optimization of approved cancer treatments

Complex treatments and outcomes in cancer

1. Correct dosing in targeted therapies

📌 *Palbociclib (CDK4/6 Inhibitor) - Metastatic Breast Cancer*

Observation : Early dose reductions (2-3 months) due to neutropenia.

Outcome : Full-dose therapy led to better progression-free survival.

Lesson : RWD emphasized dose intensity vs. toxicity, supporting use of growth factors to maintain optimal dosing.

2. Adherence and Persistence with Oral Oncolytics

📌 *Osimertinib – EGFR + NSCLC*

Observation : ~20% of patients missed doses/stopped therapy (financial, side effects).

Outcome : High adherence (≥90% of doses) correlated with longer PFS.

Lesson: RWD revealed adherence barriers, leading to support programs & dose management strategies.

3. Off-Label Use in Oncology

📌 *Checkpoint Inhibitors - Rare Tumors*

Observation- Frequent off-label use in rare cancers (e.g., pembrolizumab, nivolumab).

Outcome : Mixed efficacy—some had prolonged remission, others saw no benefit or severe toxicities.

Lesson : RWD guided new trials & flagged safety concerns in off-label use.

Active surveillance systems

Sentinel

US FDA (2008)

DARWIN EU

Europe EMA (2022)

CNODES

CANADIAN NETWORK FOR OBSERVATIONAL DRUG EFFECT STUDIES

CANADA, 2011

3. RWD as a Game-Changer in Personalized Oncology

Personalized medicine in oncology aims to match the **right treatment to the right patient** based on individual characteristics such as genetics, tumor biology, and clinical history.

RWD to Identify Predictive Biomarkers for Therapy Response

PD-L1 Biomarkers in NSCLC Immunotherapy

- High PD-L1 (≥50%) → Strong response to first-line pembrolizumab, reducing chemotherapy use.
- Low PD-L1 (<1%) → Lower response, supporting combination therapy strategies.

Enhancing Treatment Selection in Precision Oncology

CDK4/6 Inhibitors in HR+/HER2- Breast Cancer

- Higher response in premenopausal women with aggressive tumors.
- Elderly patients (>75 years) face more toxicity, supporting lower starting doses.

Predicting Immunotherapy Toxicity Using RWD

Checkpoint Inhibitors (PD1/PD-L1 inhibitors)

- Patients with pre-existing autoimmune diseases → higher risk of severe irAEs.
- Early steroid intervention reduced hospitalizations and treatment discontinuation.

Advancing Personalized Medicine with Liquid Biopsies and RWD

Detecting Resistance in Colorectal and Lung Cancer

- Liquid biopsies can detect EGFR resistance mutations earlier than traditional biopsies.
- CC patients with acquired KRAS mutations post-treatment may benefit from switching to alternative targeted therapies.

4. The Future of RWD in Oncology – Challenges and Solutions

Challenges

- ❑ Data Quality and Completeness issues
  - Missing or Incomplete Data
  - Data Entry Errors
  - Limited Longitudinal Tracking (gaps in follow-up data)

- ❑ Data Integration and Interoperability Challenges
  - Heterogeneous Data Sources
  - Lack of Data Standardization
  - Difficulty Linking Data Across Sources

- ❑ Selection Bias and Data Representativeness
  - Underrepresentation of Minority and Rural Populations
  - Selection Bias in EHR-Based Studies
  - Lack of Randomization & Confounding Factors.

Response evaluation criteria

Regulatory and Compliance

Cost and Resource Constraints

Potential solutions

- ✓ Structured reporting templates for oncology data.
- ✓ Standardized terminologies – ICD-10, SNOMED, LOINC, OMOP
- ✓ Automated Data entry and imputation with AI and NLP

- ✓ Adoption of FHIR (Fast Healthcare Interoperability Resources)
- ✓ Integrate EHRs, insurance claims, genomic sequencing data, and patient registries to fill data gaps – Cancer LinQ initiative.
- ✓ SEER-Medicare Linked Dataset, MIT's MedRec blockchain model.

- ✓ Expanding RWD Sources for More Representative Data - FDA's Project Baseline, ASCO's CancerLinQ
- ✓ Statistical Techniques - Propensity Score Matching (PSM), Inverse Probability Weighting (IPW), synthetic patient records to fill data gaps.

Tumor Progression Models

Framework and Laws

Pragmatic Trials

AI and automation

R programming for Real–World Evidence

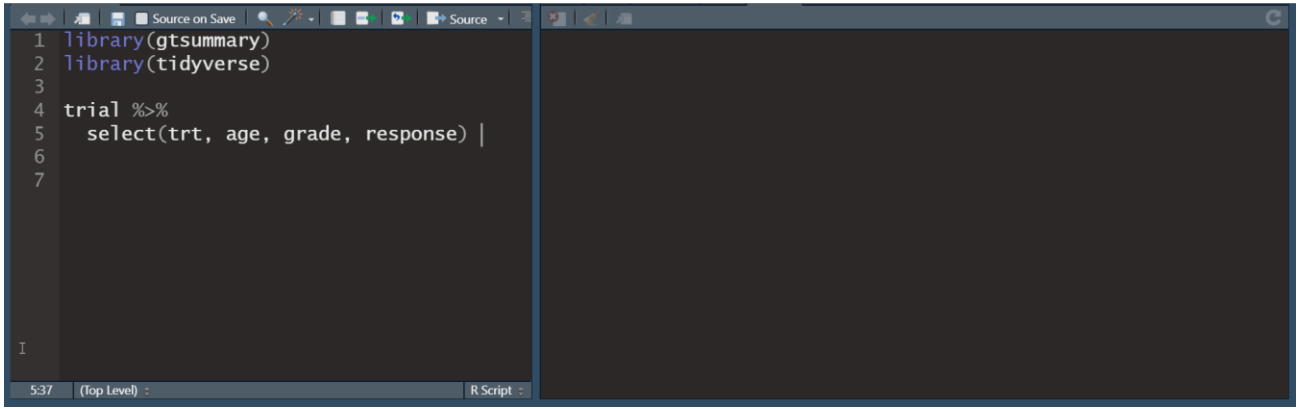
R programming for Real –World Evidence

- Open source
- Ecosystem of packages
- Reporting & Reproducible Research
- Cloud environment and integration
- Community support

- Consistent & Intuitive Syntax (%>%)
- Powerful Data Manipulation (dplyr)
- Elegant & Flexible Data Visualization (ggplot2)
- Efficient Data Cleaning & Reshaping (tidyr)
- Faster & Simpler Data Import (readr)
- Functional Programming & Iteration (purrr)

- No need to write raw SQL!
- Works with Many Databases
- Lazy Evaluation
- Optimized SQL Queries for Performance

Publication-ready summary tables for descriptive statistics, regression models, and survival analysis with gtsummary



New York Air Quality Measurements					
Ozone	Solar.R	Wind	Temp	Month	Day
41	190	7.4	67	5	1
36	118	8.0	72	5	2
12	149	12.6	74	5	3
18	313	11.5	62	5	4
		14.3	56	5	5
28		14.9	66	5	6
Daily air quality measurements in New York, May to September 1973.					
Hummm, non non rien.					

cut	price	density
Ideal	3 457.5 $	
Premium	4 584.3 $	
Good	3 928.9 $	
Very Good	3 981.8 $	
Fair	4 358.8 $	

References - https://www.danieldsjoberg.com/gtsummary/; https://davidgohel.r-universe.dev/flextable

Customizable Word Reports with R: Using Templates and Packages

officedown Example

David Gohel

2023-01-06

1. Prerequisites

This is a *sample* book written with R package **bookdown** and R package **officedown**.

The **officedown** package can be installed from CRAN or Github:

```
install.packages("officedown")
# remotes::install_github("davidgohel/officedown")
```

2. Introduction

```
ft_link <- fp_text(font.size = 9, italic = TRUE, color = "#C32900", font.family = "Cambria")
```

The purpose of this bookdown is to test the functionality of the officedown package. It contains texts of no interest but illustrates most of the functions of the package.

2.1. List demo

- This is a linked reference to Chapter 2.1.
- This is a linked reference to Chapter 4.
- This is a linked reference to Chapter 5.
- Figures and tables can have auto-numbered captions that can also be cross referenced:
  > This is a linked reference to a figure: **6-2**, its number is computed by Word and it's linked to the corresponding graphic when clicking on it.
  > This is a linked reference to a table: **4-1**, its number is computed by Word and it's linked to the corresponding table when clicking on it.

1. An item
2. An item
   2.1. An item
      2.1.1. An item
      2.1.2. An item
   2.2. An item
3. An item

4. Tables

This is famous `mtcars` dataset:

```
head(dat, n = 10)
```

Table 4-1: mtcars

car	mpg	cyl	disp	hp	drat	wt	qsec	vs	am	gear	carb
Mazda RX4	21.0	6	160.0	110	3.90	2.620	16.46	0	1	4	4
Mazda RX4 Wag	21.0	6	160.0	110	3.90	2.875	17.02	0	1	4	4
Datsun 710	22.8	4	108.0	93	3.85	2.320	18.61	1	1	4	1
Hornet 4 Drive	21.4	6	258.0	110	3.08	3.215	19.44	1	0	3	1
Hornet Sportabout	18.7	8	360.0	175	3.15	3.440	17.02	0	0	3	2
Valiant	18.1	6	225.0	105	2.76	3.460	20.22	1	0	3	1
Duster 360	14.3	8	360.0	245	3.21	3.570	15.84	0	0	3	4
Merc 240D	24.4	4	146.7	62	3.69	3.190	20.00	1	0	4	2
Merc 230	22.8	4	140.8	95	3.92	3.150	22.90	1	0	4	2
Merc 280	19.2	6	167.6	123	3.92	3.440	18.30	1	0	4	4

This is famous `iris` dataset:

```
head(iris)
```

Table 4-2: iris

Sepal.Length	Sepal.Width	Petal.Length	Petal.Width	Species
5.1	3.5	1.4	0.2	setosa
4.9	3.0	1.4	0.2	setosa
4.7	3.2	1.3	0.2	setosa
4.6	3.1	1.5	0.2	setosa
5.0	3.6	1.4	0.2	setosa
5.4	3.9	1.7	0.4	setosa

This a flextable:

Thank You

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The Global Healthcare Data Science Community

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Early detection and awareness can lower incidence and mortality rates