Meeting Specific Needs With a General Framework

Reporting Table Generation With R and 'rtables'

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Introduction

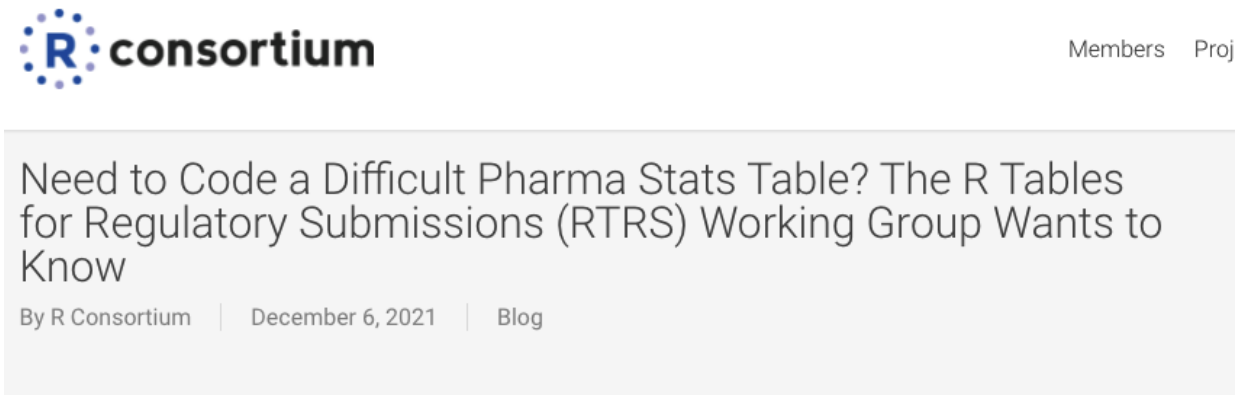
Me

- Primary developer of `rtables >= 0.2.0`
- Statistical Computing Consultant
- PhD in Statistical Computing
- Frequent collaborator with R core team
    - several new features incorporated into R

R Tables For Regulatory Submission (RTRS) Working Group

- RConsortium Formal Working Group
- Members represent
  - Multiple Pharma Companies
  - Multiple table package authors
  - US FDA
  - RStudio
- Ongoing work to assess full feature-space Pharma Tables
- Collectively Authoring “State of the Field” style lit. review

RTRS-WG Call For Difficult Tables



File issues at:
https://github.com/RConsortium/rtrs-wg/issues

rtables

`rtables` - What

R package:

- Purpose built to create reporting tables
- General across table types
- Modern expressive API

`rtables` - Why

Cornerstone piece of larger work to enable clinical trial work in R

- Tables aren't enough by themselves, but
- Can't file without tables

`rtables` - Impact at Roche

196 Internal Production Table Variant Templates Across 24 Categories

	Production Table Templates
Total	196
Adverse Event	54
Concomittant Medication	13
Demographics and Baseline	5
ECG Related	7
Lab Test	38
Other	39
Response-Related	10
Statistical Model Summary	24
Time To Event	6

`rtables` Usage In Practice

- In use in multiple active Roche trials
  - Will be used in any filings from these trials
- (Planned) All new Roche studies starting in 2023
- Powers exploratory work across many programs
  - Including those not currently using it for regulator tables

Availability

`rtables` is

- Open Source with Permissive License
- Available on CRAN
- Developed in Public
    - https://github.com/Roche/rtables
- Funded and Copyright F. Hoffmann-La Roche AG

`rtables` introduction

`rtables` Is General But Informed By Pharma's Needs

- Complex Table Structures
  - Row & Column Space
- Row-group Summaries
- "Top-left" Annotations
- Titles and Footers
- Referential Footnotes
- Pagination
- Alternate Patient Counts

Consider an AE Table

Adverse Events
By Arm, Biomarker Load and Grade

	ARM A		ARM B		All Patients	
	Low (N=78)	High (N=68)	Low (N=81)	High (N=73)	Low (N=159)	High (N=141)
Patients with >0 events	62 (79.5%)	59 (86.8%)	78 (96.3%)	72 (98.6%)	140 (88.1%)	131 (92.9%)
Total events	1042	1018	571	569	1613	1587
--Any Grade--	62	59	78	72	140	131
1	22	17	14	19	36	36
2	40	42	64	53	104	95
NERVOUS SYSTEM DISORDERS						
--Any Grade--	62	59	75	70	137	129
1	0	0	0	0	0	0
2	62	59	75	70	137	129
HEADACHE						
--Any Grade--	62	59	75	70	137	129
1	0	0	0	0	0	0
2	62	59	75	70	137	129
VASCULAR DISORDERS						
--Any Grade--	62	59	75	71	137	130
1	42	33	35	46	77	79
2	20	26	40	25	60	51
HYPOTENSION						
--Any Grade--	61	57	62	67	123	124
1	61	57	62	67	123	124
2	0	0	0	0	0	0
ORTHOSTATIC HYPOTENSION						
--Any Grade--	60	59	62	55	122	114
1	0	0	0	0	0	0
2	60	59	62	55	122	114

Starting Simple

```
l <-basic_table() %>%
    analyze("USUBJID", afun = s_events_patients)
build_table(l, ADAE2, alt_counts_df = ADSL2)
```

```
                                all obs
————————————————————————————————————
Patients with >0 events   271 (90.3%)
Total events                 3200
```

Splitting By Arm

```
l <-basic_table() %>%
    split_cols_by("ARM") %>%
    analyze("USUBJID", afun = s_events_patients)
build_table(l, ADAE2, alt_counts_df = ADSL2)
```

	ARM A	ARM B
Patients with >0 events	121 (82.9%)	150 (97.4%)
Total events	2060	1140

Counting By Grade

```
l <-basic_table() %>%
    split_cols_by("ARM") %>%
    summarize_row_groups("USUBJID",
            cfun = s_events_patients) %>%
    analyze("AETOXGR",
            afun = ids_per_grade,
            show_labels = "hidden")
build_table(l, ADAE2, alt_counts_df = ADSL2)
```

	ARM A	ARM B
Patients with >0 events	121 (82.9%)	150 (97.4%)
Total events	2060	1140
--Any Grade--	121	150
1	39	33
2	82	117

Splitting By System Organ Class

```
l <-basic_table() %>%
    split_cols_by("ARM") %>%
    summarize_row_groups("USUBJID",
            cfun = s_events_patients) %>%
    split_rows_by("AEBODSYS",
                  child_labels = "visible",
                  indent_mod = -1,
                  split_fun = trim_levels_in_group("AEDECOD")) %>%
    analyze("AETOXGR",
            afun = ids_per_grade,
            show_labels = "hidden")
build_table(l, ADAE2, alt_counts_df = ADSL2)
```

	ARM A	ARM B
Patients with >0 events	121 (82.9%)	150 (97.4%)
Total events	2060	1140
NERVOUS SYSTEM DISORDERS		
--Any Grade--	121	145
1	0	0
2	121	145
VASCULAR DISORDERS		
--Any Grade--	121	146
1	75	81
2	46	65

Splitting By Preffered Term Within SOC

```
l <-basic_table() %>%
    split_cols_by("ARM") %>%
    summarize_row_groups("USUBJID",
            cfun = s_events_patients) %>%
    split_rows_by("AEBODSYS",
                  child_labels = "visible",
                  indent_mod = -1,
                  split_fun = trim_levels_in_group("AEDECOD")) %>%
    split_rows_by("AEDECOD") %>%
    analyze("AETOXGR",
            afun = ids_per_grade,
            show_labels = "hidden")
build_table(l, ADAE2, alt_counts_df = ADSL2)
```

	ARM A	ARM B
Patients with >0 events	121 (82.9%)	150 (97.4%)
Total events	2060	1140
NERVOUS SYSTEM DISORDERS		
HEADACHE		
--Any Grade--	121	145
1	0	0
2	121	145
VASCULAR DISORDERS		
HYPOTENSION		
--Any Grade--	118	129
1	118	129
2	0	0
ORTHOSTATIC HYPOTENSION		
--Any Grade--	119	117
1	0	0
2	119	117

Summarizing SOC

```
l <-basic_table() %>%
    split_cols_by("ARM") %>%
    summarize_row_groups("USUBJID",
            cfun = s_events_patients) %>%
    split_rows_by("AEBODSYS",
                  child_labels = "visible",
                  indent_mod = -1,
                  split_fun = trim_levels_in_group("AEDECOD")) %>%
    summarize_row_groups("AETOXGR",
                         cfun = ids_per_grade) %>%
    split_rows_by("AEDECOD") %>%
    analyze("AETOXGR",
            afun = ids_per_grade,
            show_labels = "hidden")
build_table(l, ADAE2, alt_counts_df = ADSL2)
```

	ARM A	ARM B
Patients with >0 events	121 (82.9%)	150 (97.4%)
Total events	2060	1140
NERVOUS SYSTEM DISORDERS		
--Any Grade--	121	145
1	0	0
2	121	145
HEADACHE		
--Any Grade--	121	145
1	0	0
2	121	145
VASCULAR DISORDERS		
--Any Grade--	121	146
1	75	81
2	46	65
HYPOTENSION		
--Any Grade--	118	129
1	118	129
2	0	0
ORTHOSTATIC HYPOTENSION		
--Any Grade--	119	117
1	0	0
2	119	117

Adding an All Patients Column

```
l <-basic_table() %>%
    split_cols_by("ARM",
                  split_fun = add_overall_level("All Patients",
                                                first = FALSE)) %>%
    summarize_row_groups("USUBJID",
                         cfun = s_events_patients) %>%
    split_rows_by("AEBODSYS",
                  child_labels = "visible",
                  indent_mod = -1,
                  split_fun = trim_levels_in_group("AEDECOD")) %>%
    summarize_row_groups("AETOXGR",
                         cfun = ids_per_grade) %>%
    split_rows_by("AEDECOD") %>%
    analyze("AETOXGR",
            afun = ids_per_grade,
            show_labels = "hidden")
build_table(l, ADAE2, alt_counts_df = ADSL2)
```

	ARM A	ARM B	All Patients
Patients with >0 events	121 (82.9%)	150 (97.4%)	271 (90.3%)
Total events	2060	1140	3200
NERVOUS SYSTEM DISORDERS			
--Any Grade--	121	145	266
1	0	0	0
2	121	145	266
HEADACHE			
--Any Grade--	121	145	266
1	0	0	0
2	121	145	266
VASCULAR DISORDERS			
--Any Grade--	121	146	267
1	75	81	156
2	46	65	111
HYPOTENSION			
--Any Grade--	118	129	247
1	118	129	247
2	0	0	0
ORTHOSTATIC HYPOTENSION			
--Any Grade--	119	117	236
1	0	0	0
2	119	117	236

Title/Footer Annotations

```
l <-basic_table(title = "WILLOWWIND - Adverse Events By Grade",
                prov_footer = wwind_prov_stamp()) %>%
    split_cols_by("ARM",
                  split_fun = add_overall_level("All Patients",
                                                first = FALSE)) %>%
    summarize_row_groups("USUBJID",
            cfun = s_events_patients) %>%
    split_rows_by("AEBODSYS",
                  child_labels = "visible",
                  indent_mod = -1,
                  split_fun = trim_levels_in_group("AEDECOD")) %>%
    summarize_row_groups("AETOXGR",
                         cfun = ids_per_grade) %>%
    split_rows_by("AEDECOD") %>%
    analyze("AETOXGR",
            afun = ids_per_grade,
            show_labels = "hidden")
build_table(l, ADAE2, alt_counts_df = ADSL2)
```

```
WILLOWWIND - Adverse Events By Grade

————————————————————————————————————————————————————————————————————
                                ARM A        ARM B      All Patients
————————————————————————————————————————————————————————————————————
Patients with >0 events     121 (82.9%)  150 (97.4%)  271 (90.3%)
Total events                    2060         1140         3200

NERVOUS SYSTEM DISORDERS
--Any Grade--                    121          145          266
1                                  0            0            0
2                                121          145          266

    HEADACHE
    --Any Grade--                121          145          266
    1                              0            0            0
    2                            121          145          266

VASCULAR DISORDERS
--Any Grade--                    121          146          267
1                                 75           81          156
2                                 46           65          111

    HYPOTENSION
    --Any Grade--                118          129          247
    1                            118          129          247
    2                              0            0            0

    ORTHOSTATIC HYPOTENSION
    --Any Grade--                119          117          236
    1                              0            0            0
    2                            119          117          236

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file: /path/to/WILLOWWIND/aet05.R *** data snapshot: 2022-04-28 *** user: gb123
```

Referential Footnotes

```
l <-basic_table(title = "WILLOWWIND - Adverse Events By Grade",
                prov_footer = wwind_prov_stamp()) %>%
    split_cols_by("ARM",
                  split_fun = add_overall_level("All Patients",
                                                first = FALSE)) %>%
    summarize_row_groups("USUBJID",
            cfun = s_events_patients) %>%
    split_rows_by("AEBODSYS",
                  child_labels = "visible",
                  indent_mod = -1,
                  split_fun = trim_levels_in_group("AEDECOD")) %>%
    summarize_row_groups("AETOXGR",
                         cfun = ids_per_grade) %>%
    split_rows_by("AEDECOD") %>%
    analyze("AETOXGR",
            afun = ids_per_grade,
            show_labels = "hidden")
tbl_narrow <- build_table(l, ADAE2, alt_counts_df = ADSL2)
fnotes_at_path(tbl_narrow,
               c("AEBODSYS", "NERVOUS SYSTEM DISORDERS",
                 "AEDECOD", "HEADACHE")) <- "Non-migraine"
tbl_narrow
```

WILLOWWIND - Adverse Events By Grade

	ARM A	ARM B	All Patients
Patients with >0 events	121 (82.9%)	150 (97.4%)	271 (90.3%)
Total events	2060	1140	3200
NERVOUS SYSTEM DISORDERS			
--Any Grade--	121	145	266
1	0	0	0
2	121	145	266
HEADACHE {1}			
--Any Grade--	121	145	266
1	0	0	0
2	121	145	266
VASCULAR DISORDERS			
--Any Grade--	121	146	267
1	75	81	156
2	46	65	111
HYPOTENSION			
--Any Grade--	118	129	247
1	118	129	247
2	0	0	0
ORTHOSTATIC HYPOTENSION			
--Any Grade--	119	117	236
1	0	0	0
2	119	117	236

{1} - Non-migraine

file: /path/to/WILLOWWIND/aet05.R *** data snapshot: 2022-04-28 *** user: gb123

The Culmination

```
l <-basic_table(title = "WILLOWWIND - Adverse Events By Grade",
                prov_footer = wwind_prov_stamp()) %>%
    split_cols_by("ARM",
                  split_fun = add_overall_level("All Patients",
                                                first = FALSE)) %>%
    split_cols_by("BMRKR") %>%
    summarize_row_groups("USUBJID",
            cfun = s_events_patients) %>%
    split_rows_by("AEBODSYS",
                  split_fun = trim_levels_in_group("AEDECOD"),
                  child_labels = "visible",
                  indent_mod = -1) %>%
    summarize_row_groups("AETOXGR",
                         cfun = ids_per_grade) %>%
    split_rows_by("AEDECOD") %>%
    analyze("AETOXGR",
            afun = ids_per_grade,
            show_labels = "hidden")
tbl <- build_table(l, ADAE2, alt_counts_df = ADSL2)
fnotes_at_path(tbl,
               c("AEBODSYS", "NERVOUS SYSTEM DISORDERS",
                 "AEDECOD", "HEADACHE")) <- "Non-migraine"
tbl
```

The Table

WILLOWWIND - Adverse Events By Grade

	ARM A		ARM B		All Patients	
	Low	High	Low	High	Low	High
Patients with >0 events	62 (79.5%)	59 (86.8%)	78 (96.3%)	72 (98.6%)	140 (88.1%)	131 (92.9%)
Total events	1042	1018	571	569	1613	1587
NERVOUS SYSTEM DISORDERS						
--Any Grade--	62	59	75	70	137	129
1	0	0	0	0	0	0
2	62	59	75	70	137	129
HEADACHE {1}						
--Any Grade--	62	59	75	70	137	129
1	0	0	0	0	0	0
2	62	59	75	70	137	129
VASCULAR DISORDERS						
--Any Grade--	62	59	75	71	137	130
1	42	33	35	46	77	79
2	20	26	40	25	60	51
HYPOTENSION						
--Any Grade--	61	57	62	67	123	124
1	61	57	62	67	123	124
2	0	0	0	0	0	0
ORTHOSTATIC HYPOTENSION						
--Any Grade--	60	59	62	55	122	114
1	0	0	0	0	0	0
2	60	59	62	55	122	114

{1} - Non-migraine

file: /path/to/WILLOWWIND/aet05.R *** data snapshot: 2022-04-28 *** user: gb123

Table Layout Code Is Naturally Parameterized

Table Structure

```
l <-basic_table(title = "WILLOWWIND - Adverse Events By Grade",
                prov_footer = wwind_prov_stamp()) %>%
    split_cols_by("ARM",
                  split_fun = add_overall_level("All Patients",
                                                first = FALSE)
                  ) %>%
    split_cols_by("BMRKR") %>%
    summarize_row_groups("USUBJID",
            cfun = s_events_patients) %>%
    split_rows_by("AEBODSYS",
                  split_fun = trim_levels_in_group("AEDECOD"),
                  child_labels = "visible",
                  indent_mod = -1) %>%
    summarize_row_groups("AETOXGR",
                         cfun = ids_per_grade) %>%
    split_rows_by("AEDECOD") %>%
    analyze("AETOXGR",
            afun = ids_per_grade,
            show_labels = "hidden")
tbl <- build_table(l, ADAE2, alt_counts_df = ADSL2)
```

Business Logic

```
l <-basic_table(title = "WILLOWWIND - Adverse Events By Grade",
                prov_footer = wwind_prov_stamp()) %>%
    split_cols_by("ARM",
                  split_fun = add_overall_level("All Patients",
                                                first = FALSE)
                  ) %>%
    split_cols_by("BMRKR") %>%
    summarize_row_groups("USUBJID",
            cfun = s_events_patients) %>%
    split_rows_by("AEBODSYS",
                  split_fun = trim_levels_in_group("AEDECOD"),
                  child_labels = "visible",
                  indent_mod = -1) %>%
    summarize_row_groups("AETOXGR",
                         cfun = ids_per_grade) %>%
    split_rows_by("AEDECOD") %>%
    analyze("AETOXGR",
            afun = ids_per_grade,
            show_labels = "hidden")
tbl <- build_table(l, ADAE2, alt_counts_df = ADSL2)
```

Multi-target Tables

```
l <-basic_table() %>%
    split_cols_by("ARM") %>%
    summarize_row_groups("USUBJID",
            cfun = s_events_patients) %>%
    analyze("AETOXGR",
            afun = ids_per_grade,
            show_labels = "hidden")
tbl <- build_table(l, ADAE2, alt_counts_df = ADSL2)
tbl
```

	ARM A	ARM B
Patients with >0 events	121 (82.9%)	150 (97.4%)
Total events	2060	1140
--Any Grade--	121	150
1	39	33
2	82	117

```
## for now helper I wrote, coming to rtables API soon
set_format_at_path(tbl, c("root",
                          "@content", "pat_count"),
                   format = "xx (xx.xx%)")
```

	ARM A	ARM B
Patients with >0 events	121 (82.88%)	150 (97.40%)
Total events	2060	1140
--Any Grade--	121	150
1	39	33
2	82	117

```
set_format_at_path(tbl, c("root",
                          "@content", "pat_count"),
                   format = "xx (xx.%)")
```

	ARM A	ARM B
Patients with >0 events	121 (83%)	150 (97%)
Total events	2060	1140
--Any Grade--	121	150
1	39	33
2	82	117

Pagination

```
pagtbl <- paginate_table(tbl_narrow, lpp = 35)
pagtbl[[1]]
```

```
WILLOWWIND - Adverse Events By Grade

_____________________________________________________________
                            ARM A       ARM B      All Patients
_____________________________________________________________
Patients with >0 events   121 (82.9%)  150 (97.4%)  271 (90.3%)
Total events                 2060        1140         3200

NERVOUS SYSTEM DISORDERS
--Any Grade--                 121         145          266
1                               0           0            0
2                             121         145          266

    HEADACHE {1}
    --Any Grade--             121         145          266
    1                           0           0            0
    2                         121         145          266

VASCULAR DISORDERS
--Any Grade--                 121         146          267
1                              75          81          156
2                              46          65          111

    HYPOTENSION
    --Any Grade--             118         129          247
    1                         118         129          247
    2                           0           0            0

_____________________________________________________________

{1} - Non-migraine
_____________________________________________________________

file: /path/to/WILLOWWIND/aet05.R *** data snapshot: 2022-04-28 *** user: gb123
```

```
pagtbl[[2]]
```

```
WILLOWWIND - Adverse Events By Grade

_____________________________________________________________
                            ARM A       ARM B      All Patients
_____________________________________________________________
Patients with >0 events   121 (82.9%)  150 (97.4%)  271 (90.3%)
Total events                 2060        1140         3200

VASCULAR DISORDERS
--Any Grade--                 121         146          267
1                              75          81          156
2                              46          65          111

    ORTHOSTATIC HYPOTENSION
    --Any Grade--             119         117          236
    1                           0           0            0
    2                         119         117          236

_____________________________________________________________

file: /path/to/WILLOWWIND/aet05.R *** data snapshot: 2022-04-28 *** user: gb123
```

Page-by Splitting

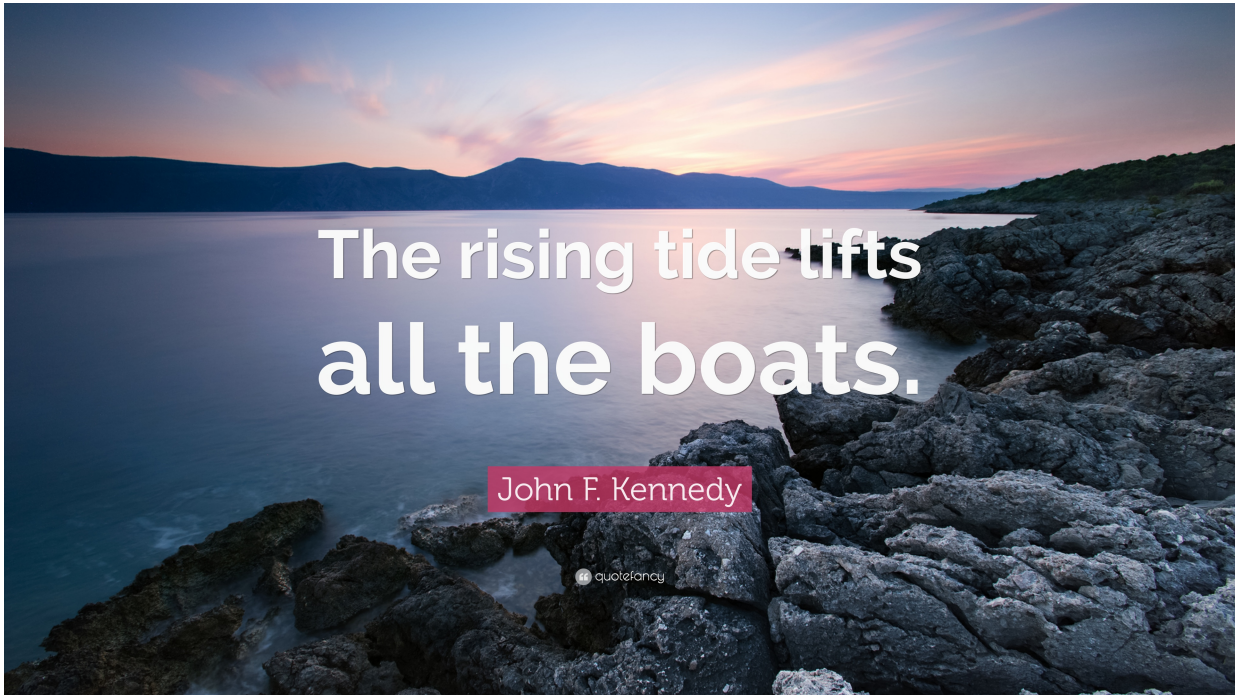
```
l <-basic_table(title = "WILLOWWIND - Adverse Events By Grade",
                prov_footer = wwind_prov_stamp()) %>%
    split_cols_by("ARM",
                  split_fun = add_overall_level("All Patients",
                                                first = FALSE)) %>%
    split_rows_by("BMRKR", page_by=TRUE) %>%
    split_rows_by("AEBODSYS",
                  split_fun = trim_levels_in_group("AEDECOD"),
                  child_labels = "visible",
                  indent_mod = -1) %>%
    analyze("AETOXGR",
            afun = ids_per_grade,
            show_labels = "hidden")
tbl <- build_table(l, ADAE2, alt_counts_df = ADSL2)
ptbl <- paginate_table(tbl, lpp = 35)
ptbl[[1]]
```

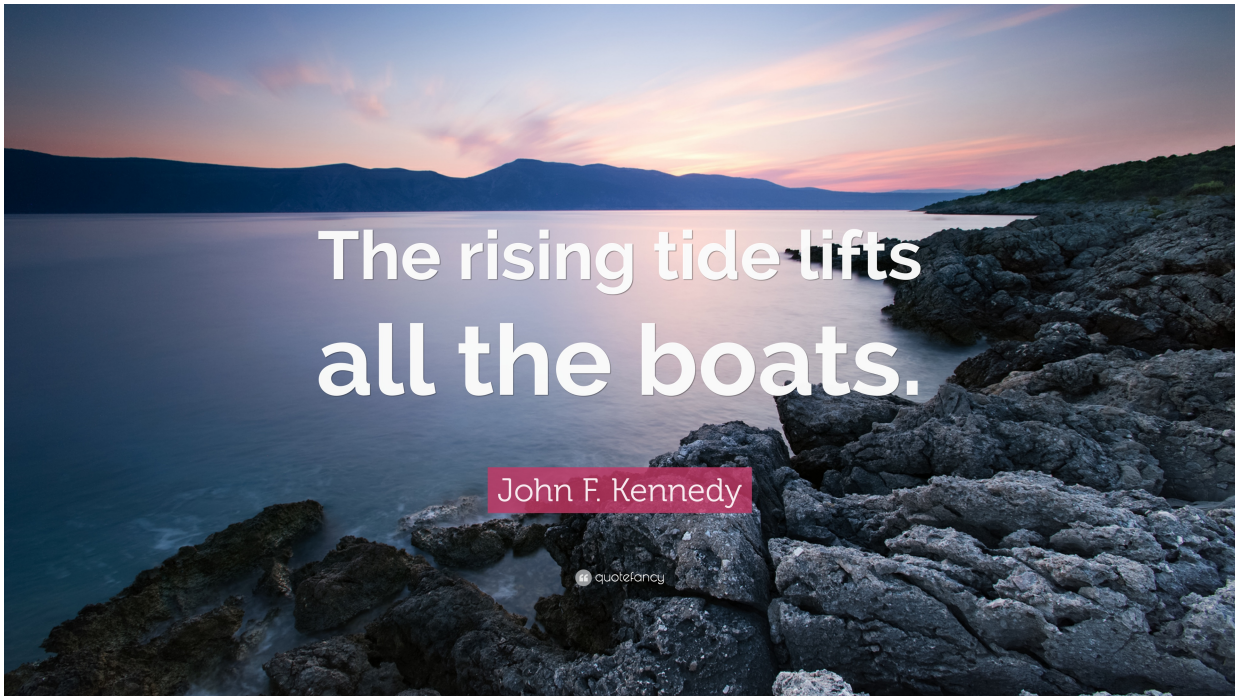
```
WILLOWWIND - Adverse Events By Grade
BMRKR: Low

_____________________________________________________
                          ARM A   ARM B   All Patients
_____________________________________________________
NERVOUS SYSTEM DISORDERS
--Any Grade--              62      75        137
1                           0       0         0
2                          62      75        137

VASCULAR DISORDERS
--Any Grade--              62      75        137
1                          42      35         77
2                          20      40         60

_____________________________________________________

file: /path/to/WILLOWWIND/aet05.R *** data snapshot: 2022-04-28 *** user: gb123
```

```
ptbl[[2]]
```

```
WILLOWWIND - Adverse Events By Grade
BMRKR: High

_____________________________________________________
                          ARM A   ARM B   All Patients
_____________________________________________________
NERVOUS SYSTEM DISORDERS
--Any Grade--              59      70        129
1                           0       0         0
2                          59      70        129

VASCULAR DISORDERS
--Any Grade--              59      71        130
1                          33      46         79
2                          26      25         51

_____________________________________________________

file: /path/to/WILLOWWIND/aet05.R *** data snapshot: 2022-04-28 *** user: gb123
```

Abstraction and Types of Effort


The rising tide lifts
all the boats.
John F. Kennedy
quotefancy



Not always, but it ***can***

Types of Effort In Creating Tables

- Front Line Work - SPAs
- SPA-Enabling Develoment (SMEs)
- Core/general Tooling Development

SPAs

- Responsible for ultimate creation of tables
- Use templates and other tools provided to them
- Creation of Ad-hoc Tables
- “Last-Mile Delivery”

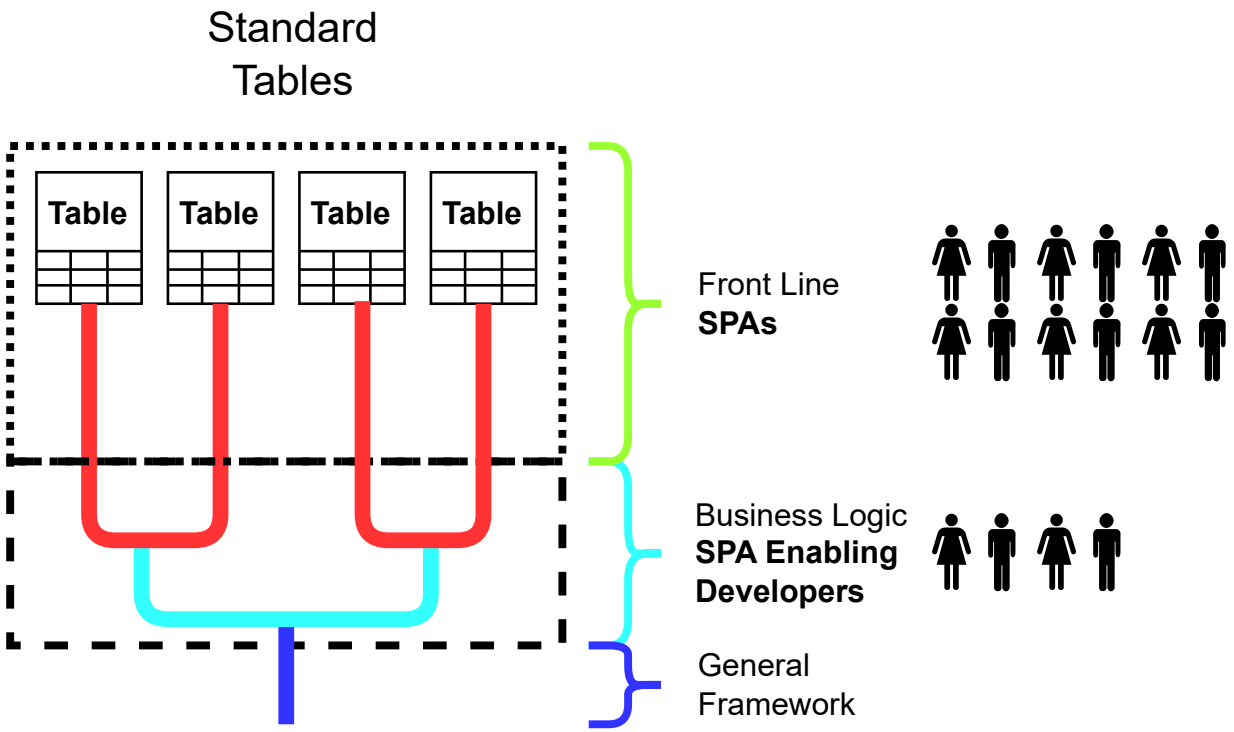
SMEs - SPA Enabling Tool Developers

- Develop table templates/functions
- Business and Statistical Logic
    - for standard tables

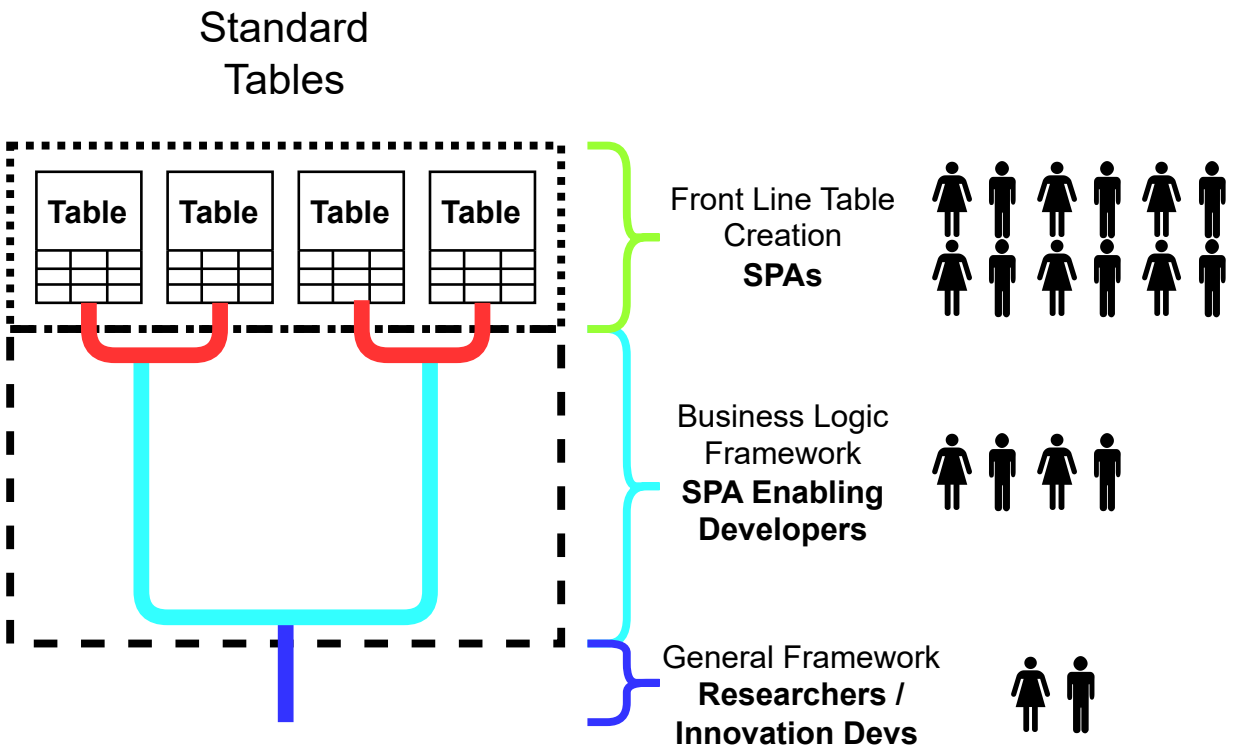
Core Table Framework

- Provide building blocks and tools that SMEs use
- Not targeted specifically at any particular table endpoint

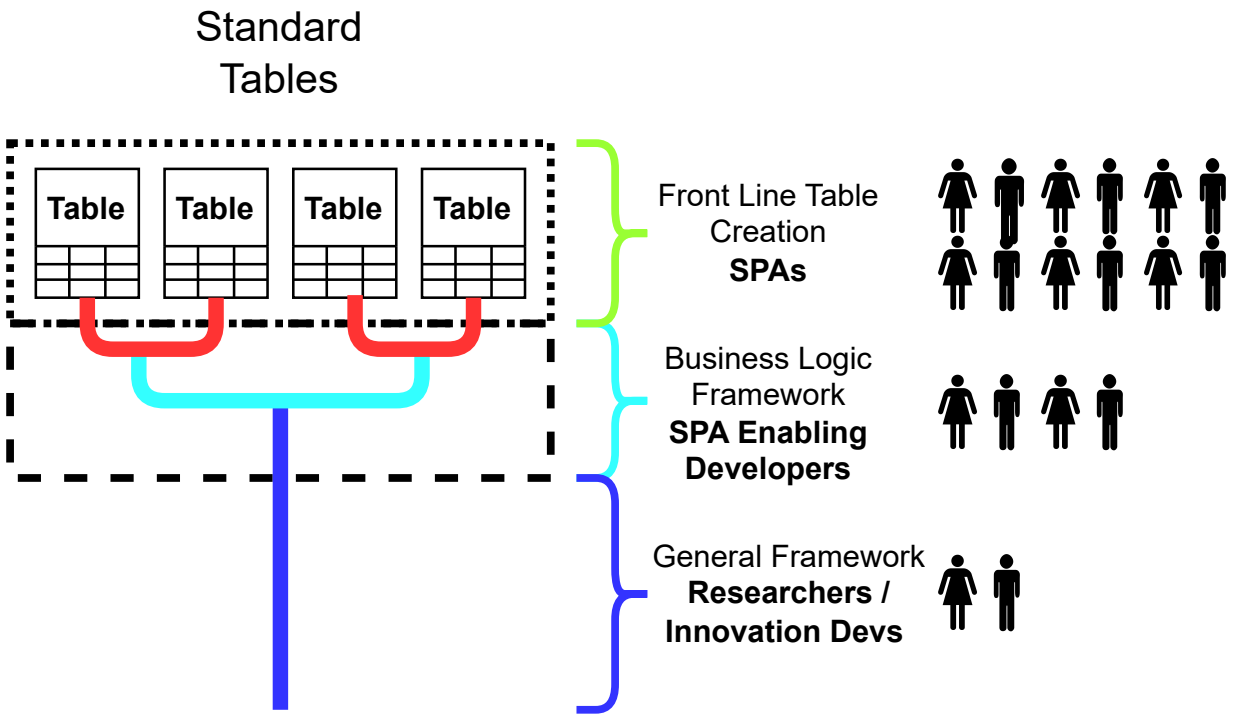
Largely Unsupported SPAs



Robust Spa-Enabling Dev Efforts



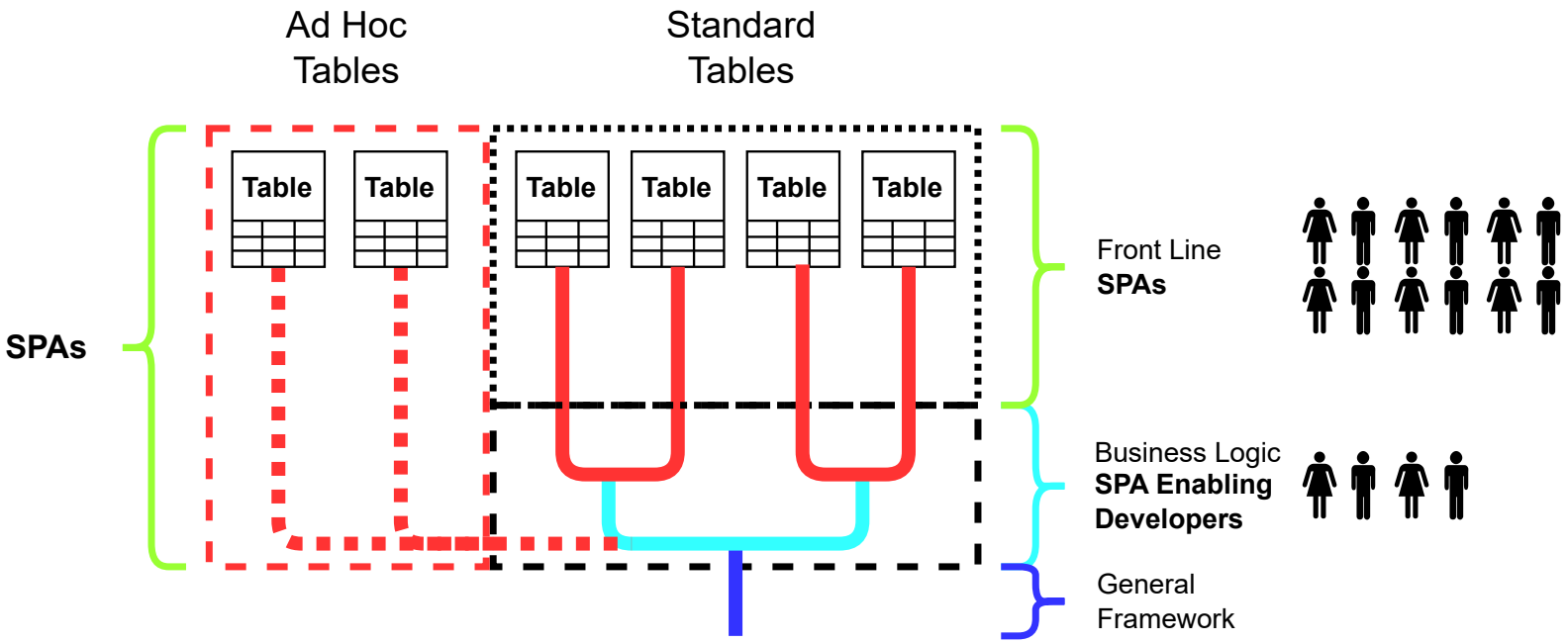
Basic Research/Innovation Supporting SMEs



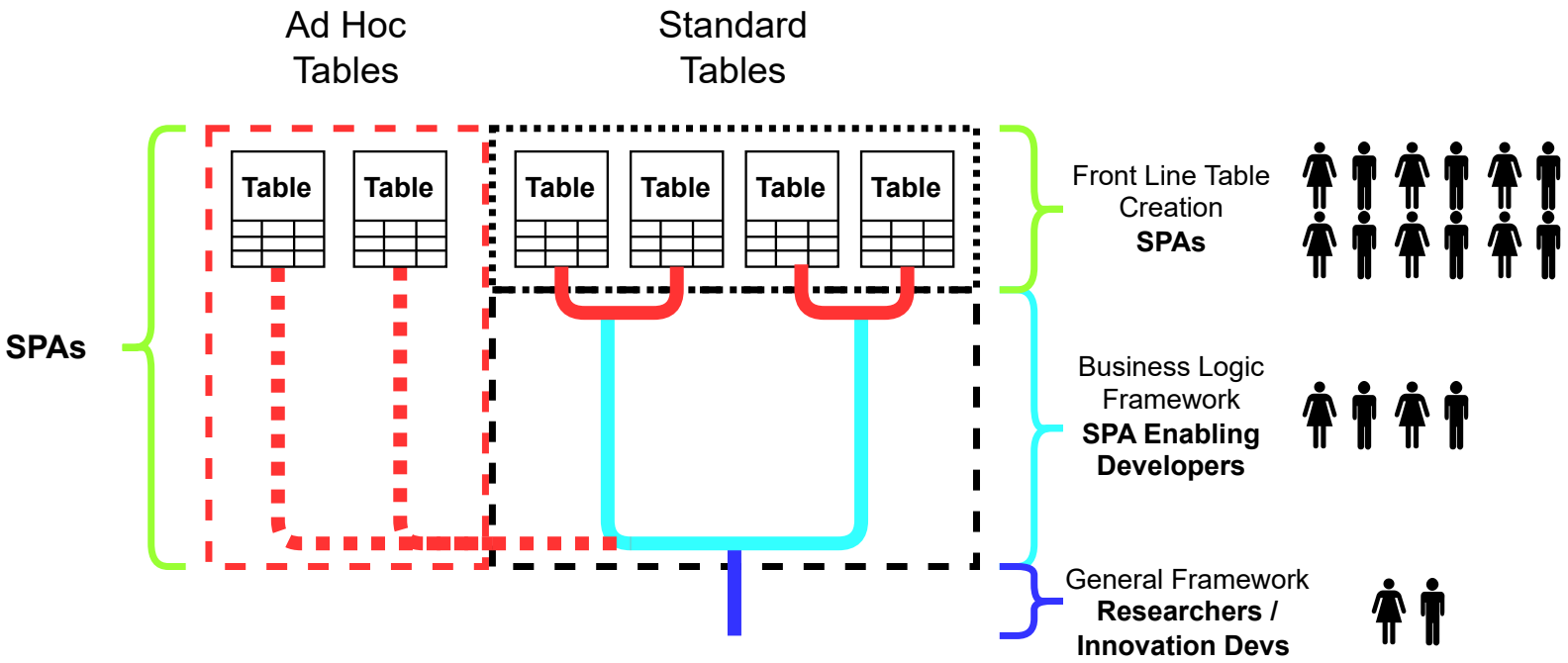
Beware


SOMETHING
Ad Hoc
wicked
THIS WAY
COMES

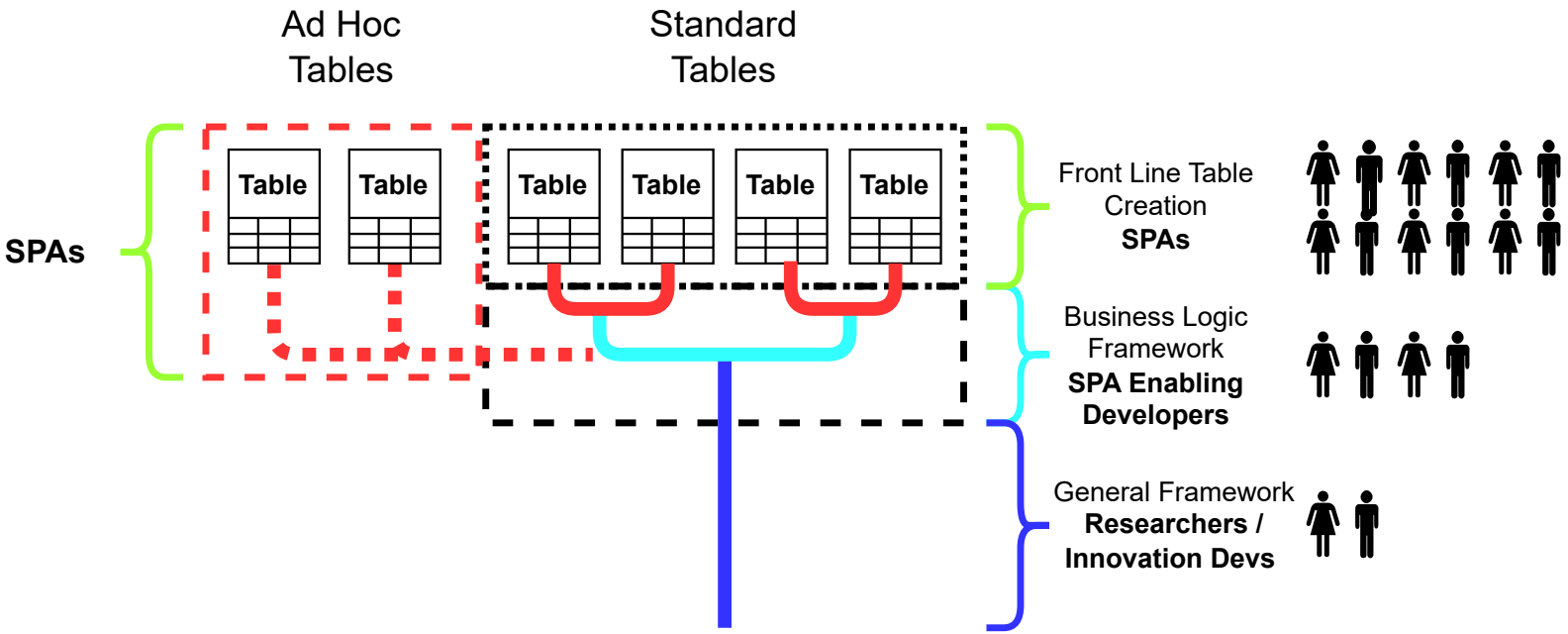
Largely Unsupported SPAs



Robust Spa-Enabling Dev Efforts

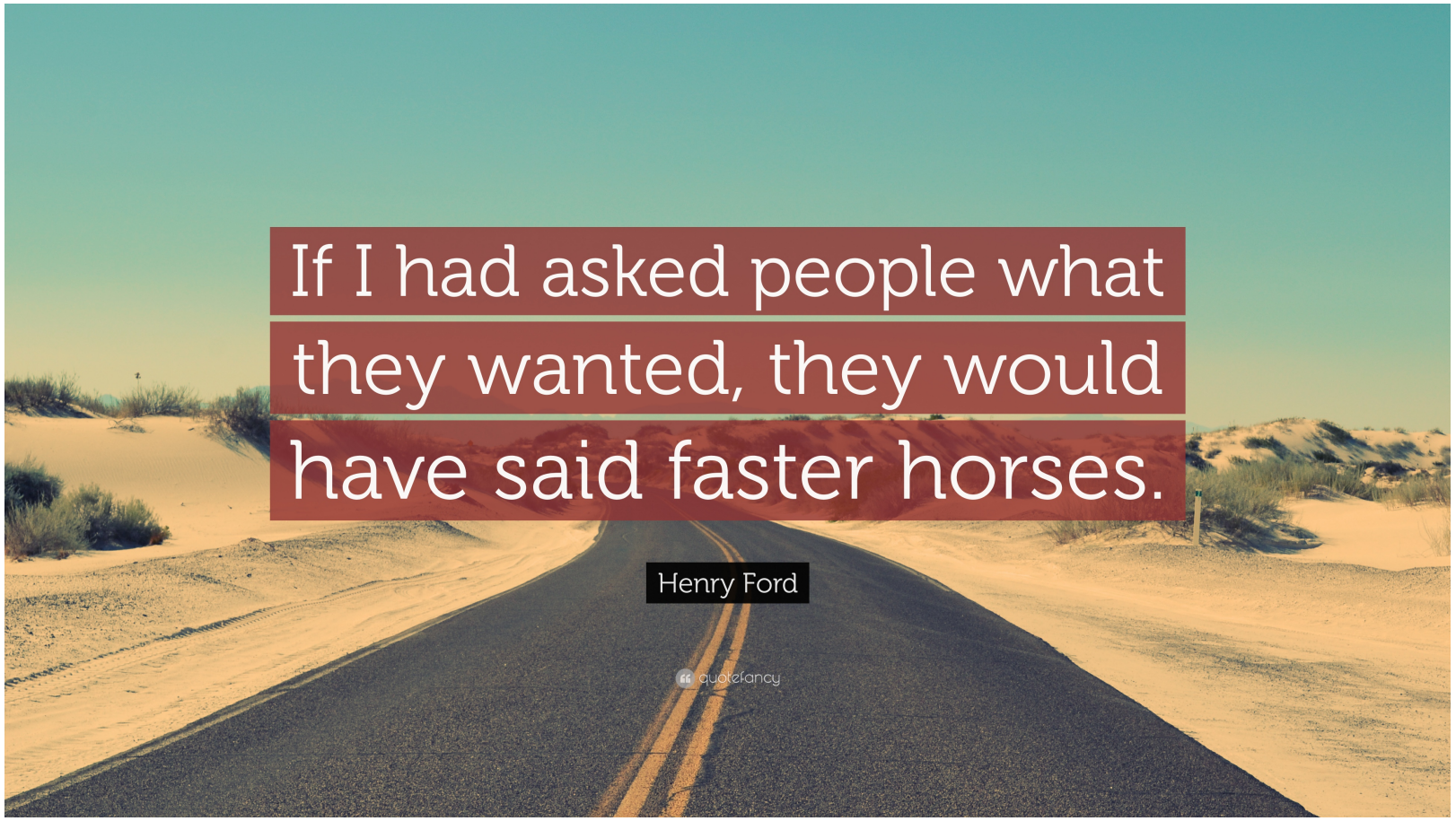


Basic Research/Innovation Supporting SMEs



Research, Innovation, and Stakeholder Needs

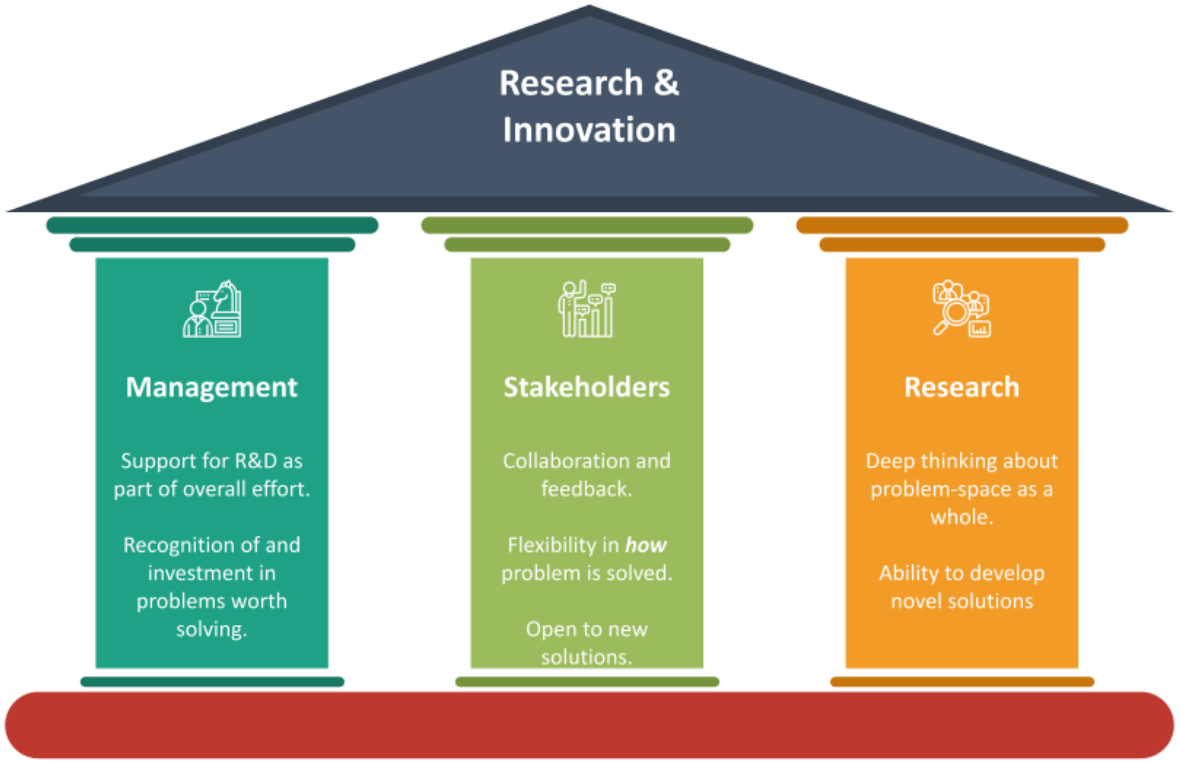
The Apocryphal Henry Ford



`rtables` Is Not Faster Horses

- New (to R) way to make tables
- Result of novel statistical computing research

Three Pillars of How We Got Here



Management Support

Upper Management

- Support POs and Tech Leads
  - Trust them to identify and pursue innovation

NEST Leadership

- Then Adrian Waddell (TL) and Tad Lewandowski (PO)
  - Saw importance of tables as both need and opportunity
  - Devoted NEST efforts to innovate in table space
  - Narrow, applied research program
    - ***within larger NEST product***
- Now continued by Pawel Rucki (TL) and Jaime Pires (PO)

Stakeholders - SME Team

- Responsible for table template creation
  - Formal goal of 200 tables during 2020
- Communicated *what* they needed, **flexible on the how**
- Willing to invest in learning new way of making tables
  - resulting in **invaluable** feedback on API, capabilities, etc

Research - `rtables` Team

- Not responsible for delivery of any given table
  - frees us to think about tables as a whole
- Asked SMEs **what they need to be able to do**
  - not how it should let them do it
- Direct frequent collaboration with SME team
  - tight feedback loop
  - what works, what doesn't, what's still missing

Knock Down Any of the Pillars

`rtables` doesn’t end up where it is now.

Next Steps

Whats Next For `rtables`

- Collaboration with RStudio on tgen
  - Multi output-format table renderer
    - rtf, HTML, etc
  - Visual formatting of tables
    - color, bolding, etc
- New features of `rtables`
  - QC-targeting table comparison functionality