18th April 2024 ESG working group in automation and technological advancement

Use of R for systematic reviews: automation, visualisation, and meta-analysis

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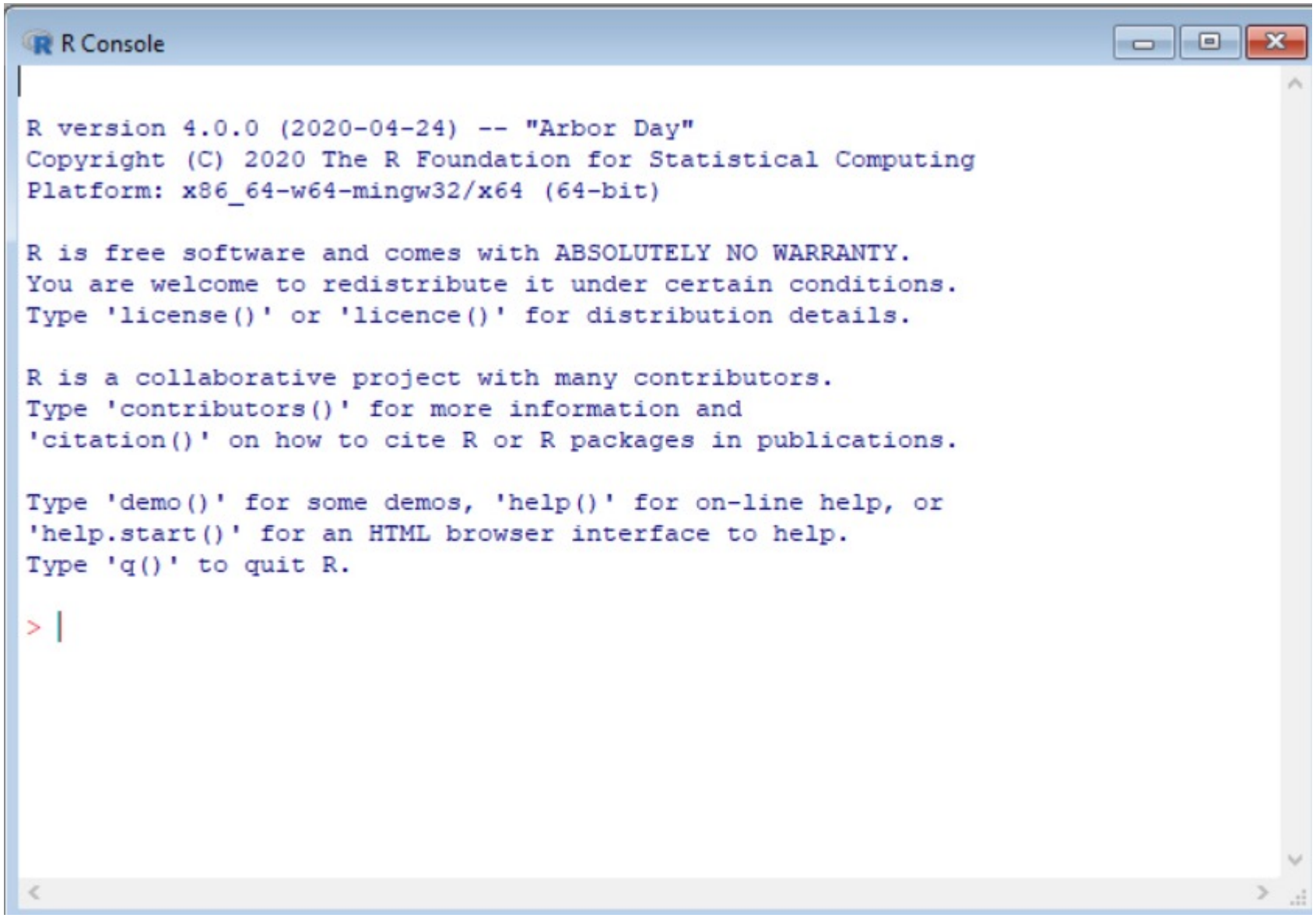
Acknowledgements for slides / content: Clareece Nevill & Janion Nevill

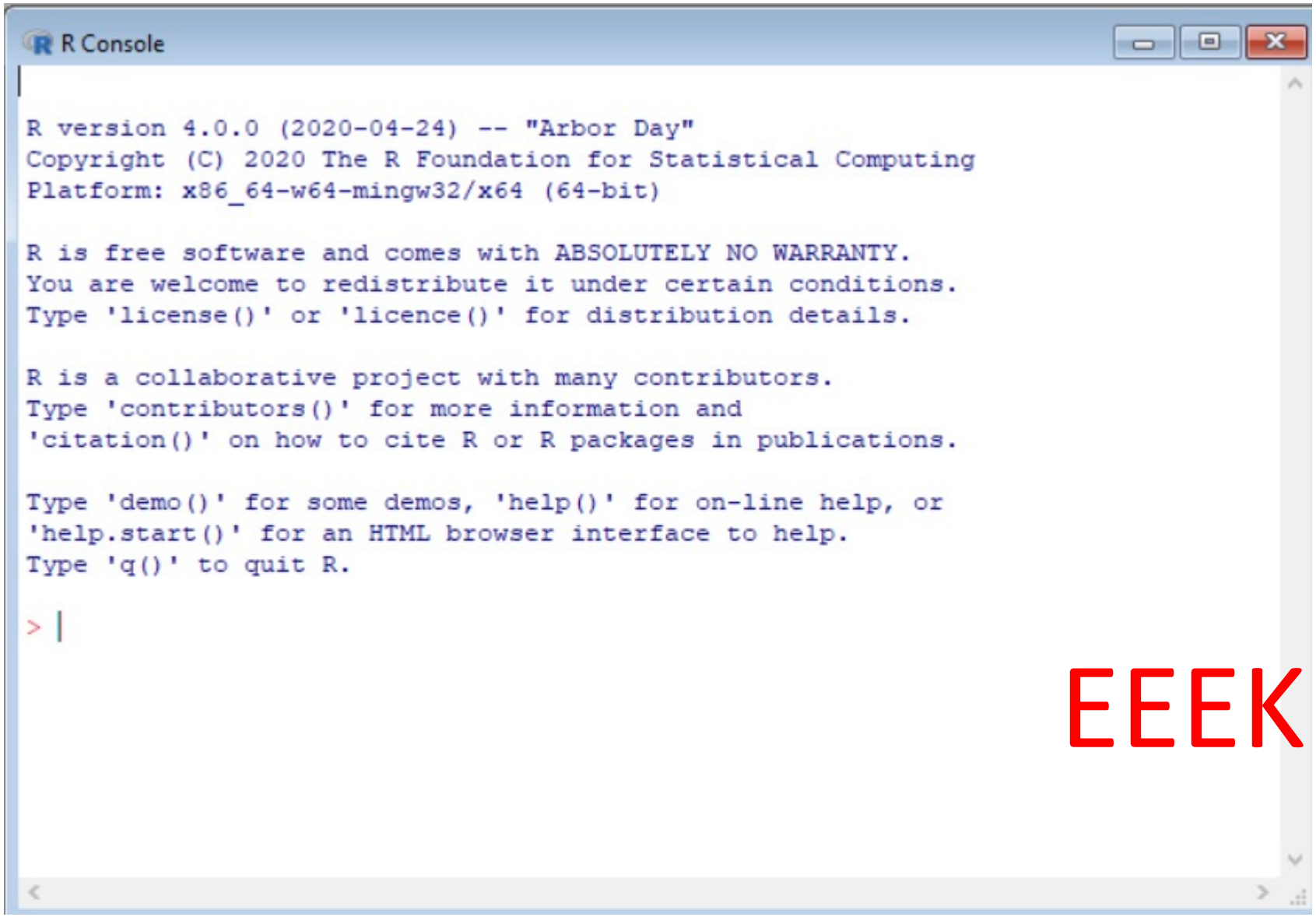
What is “R”?

- R was created in the early 1990s by University of Auckland statisticians Ross Ihaka and Robert Gentleman (https://www.r-project.org/)
- R draws heavily on parent computer language S, which was originally developed by Bell Telephone Laboratories in the 1970s
  - Interactive approach to statistical computing
  - S and then S+ were both commercial, R is free and now dominates
- Capabilities of R have been expanded over the years
  - 20,000+ packages to download to extend functionality
  - Some packages, e.g. Tidyverse seen as all but essential in how they expand and improve R’s functionality (https://www.tidyverse.org/)

What does R look like?



What does R look like?



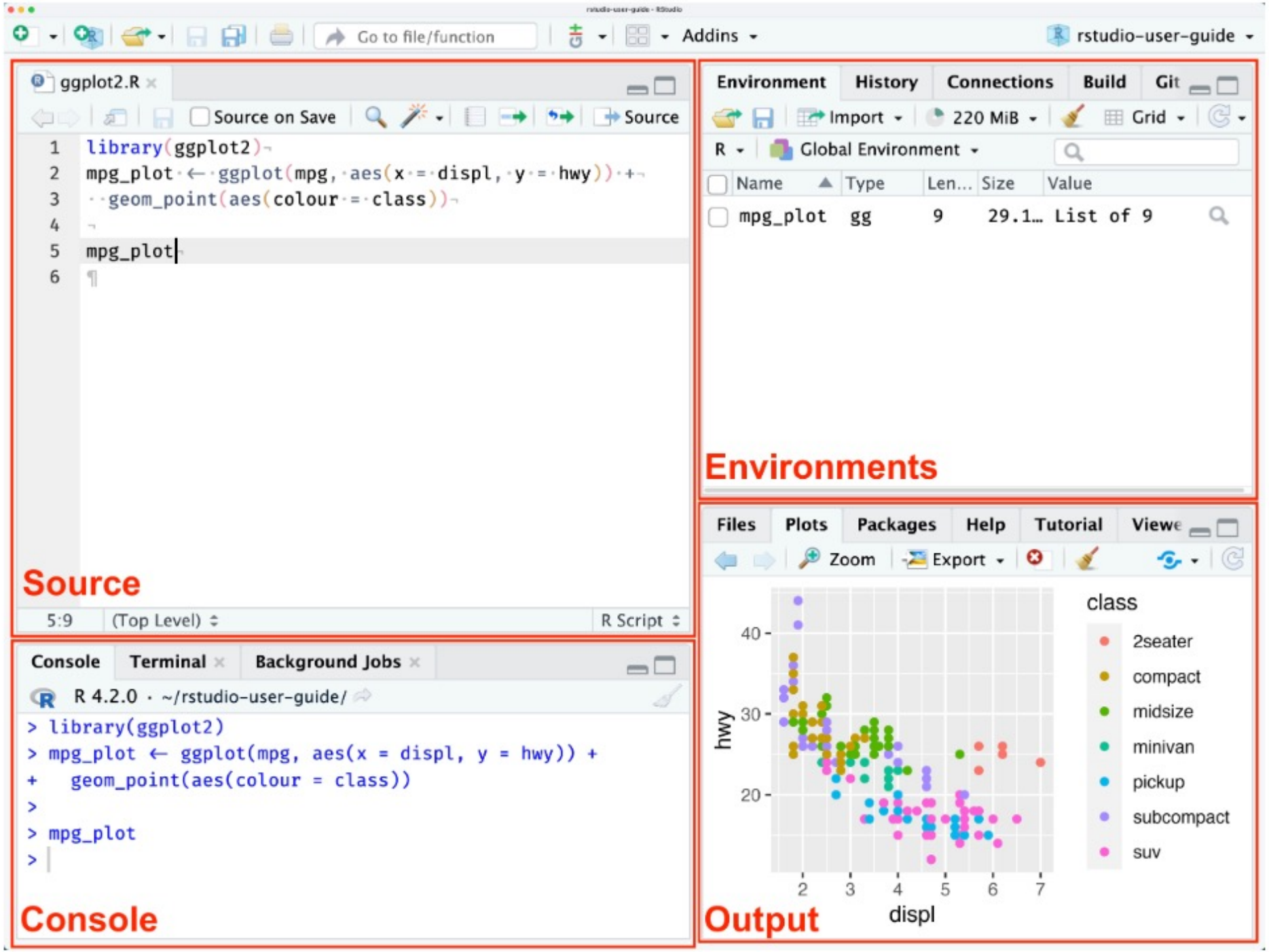
EEEK!!

RStudio

- Rstudio – “an integrated development environment for R”
- Developed by Posit (formally Rstudio) (https://posit.co/download/rstudio-desktop/)
- Desktop and Web versions

RStudio

- There is a lot of material online for anyone that wants to learn R/RStudio



How can R help with Systematic Reviews?

https://esmarconf.org/

- ESMARConf is a FREE, online annual conference series dedicated to evidence synthesis and meta-analysis in R.

Aim is to raise awareness of the utility of Open Source tools in R for conducting all aspects of evidence syntheses (systematic reviews/maps, meta-analysis, rapid reviews, scoping reviews, etc.), to build capacity for conducting rigorous evidence syntheses, to support the development of novel tools and frameworks for robust evidence synthesis, and to support a community of practice working in evidence synthesis tool development.

Run 3 times to date (next one in 2025)

All sessions have been recorded and curated https://esmarconf.org/recordings/

Early Stages of a Systematic Review

Study retrieval

- GSscraper (https://youtu.be/unUOUpG8dOg)
  - Scrapes search from Google Scholar
- citationchaser (https://youtu.be/pyt2YgPUVfs)
  - Forward & backwards citation utility

Study screening & deduplication

- revtools (https://youtu.be/WMpPCvBeILQ)
- screenmedR (https://youtu.be/7SWoQSvDgWY)
  - Article screening
- ASySD (https://youtu.be/WL0VDgxcUNE)
  - Identifies duplicate publications
- CiteSource (https://youtu.be/xBW1wQDHk5g)
  - Analysis of sources, methods and search strategies

Meta-analysis

- There are an overwhelming number of R packages that perform some aspect of meta-analysis
- A curated and frequently updated list is available :
  - https://cran.r-project.org/web/views/MetaAnalysis.html
- Also see ESMAR Conf talks (previous slides)

** Alex Go To Website **

‘Standard’ Meta-Analysis packages

- {Metafor} (https://www.metafor-project.org/) by Wolfgang Viechtbauer
  - Extensive functionality
  - Well documented and maintained
  - Actively developed
  - Recently added automated report writing functionality(!) (https://www.youtube.com/watch?v=gAc66E4r-aU)

- {Meta} (https://cran.r-project.org/web/packages/meta/index.html) by Guido Schwarzer
  - A good alternative
  - Well documented and maintained
  - Actively developed

******** Alex go to Metafor webpage ******

Network Meta Analysis

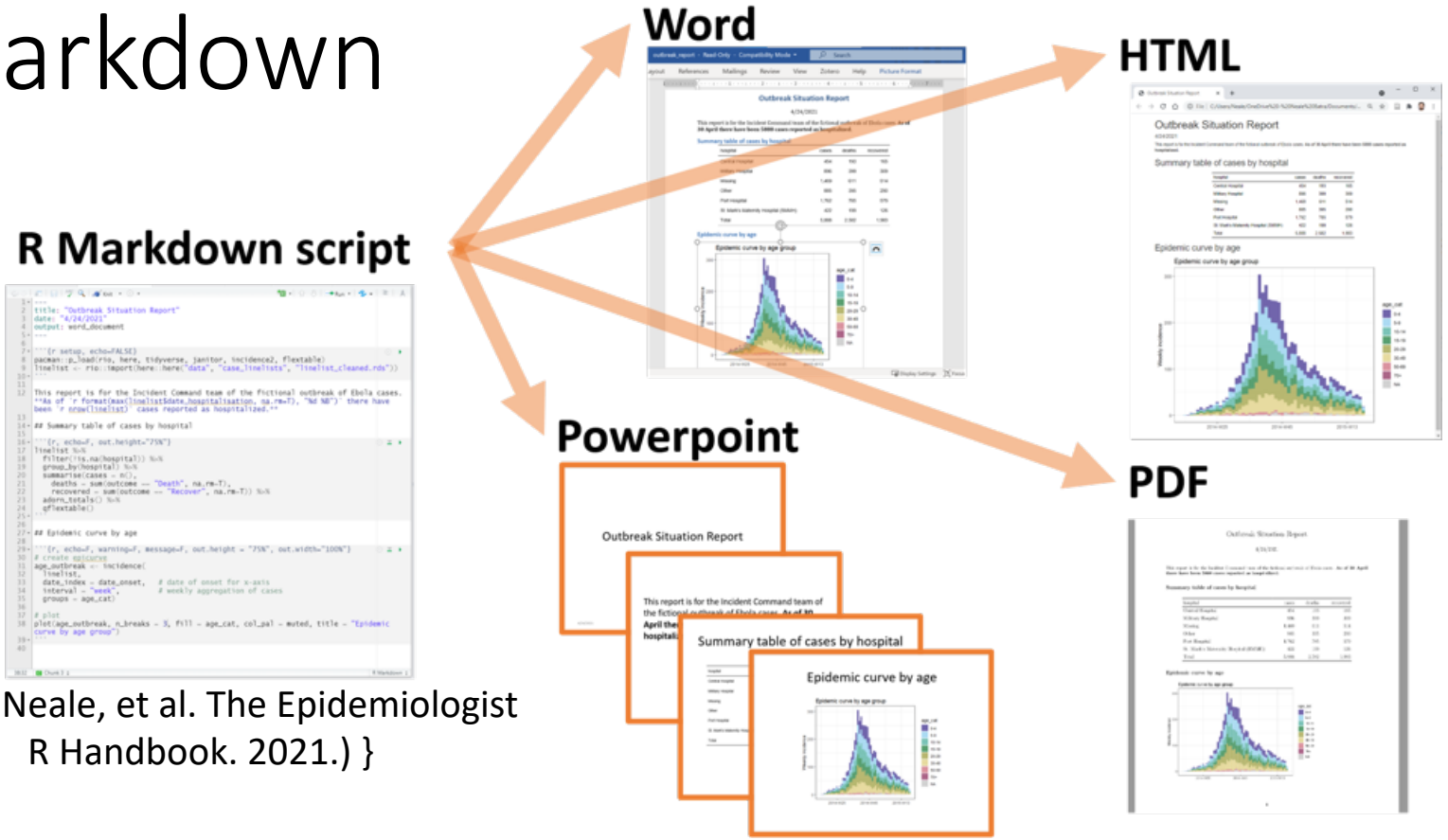
- A number of options available including

- {netmeta} by Rücker et al. (https://cran.r-project.org/web/packages/netmeta/index.html)
  - Frequentist methods
  - Actively developed and maintained

- {gemtc} by Gert van Valkenhoef, Joel Kuiper (https://cran.r-project.org/web/packages/gemtc/index.html)
  - Bayesian methods (which call another program WinBUGS / JAGS)
  - Very clever inconsistency assessment routine
  - Maintained but not actively developed

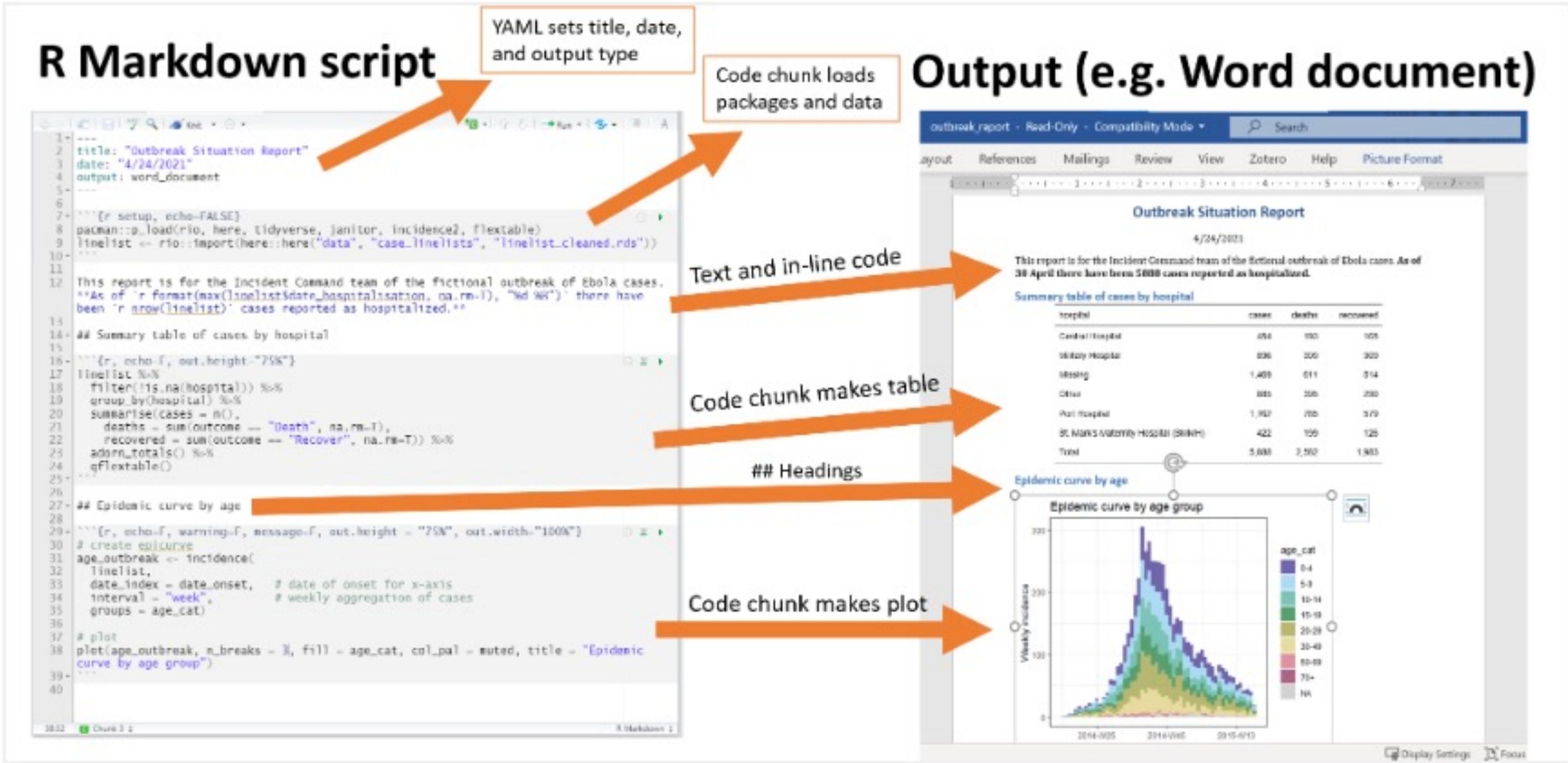
- {Multinma} by David Phillippo (https://cran.r-project.org/web/packages/multinma/index.html)
  - Bayesian methods (which call STAN software)
  - Relatively new, maintained and actively developed
  - Allows incorporation if individual patient data

Report Writing: R Markdown



(Batra, Neale, et al. The Epidemiologist R Handbook. 2021.) }

- It is possible to write papers / books / webpages etc without leaving R
- But why would you ever want to do any scientific writing in R??
  1. It is elegant for annotating output to communicate to others
  2. Data, analysis code and output can be contained within a report file
     - Transparent
     - Reproducible
     - Easy to update / produce routine reports (living systematic reviews anyone?)



(Batra, Neale, et al. The Epidemiologist R Handbook. 2021.) https://epirhandbook.com/en/reports-with-r-markdown.html

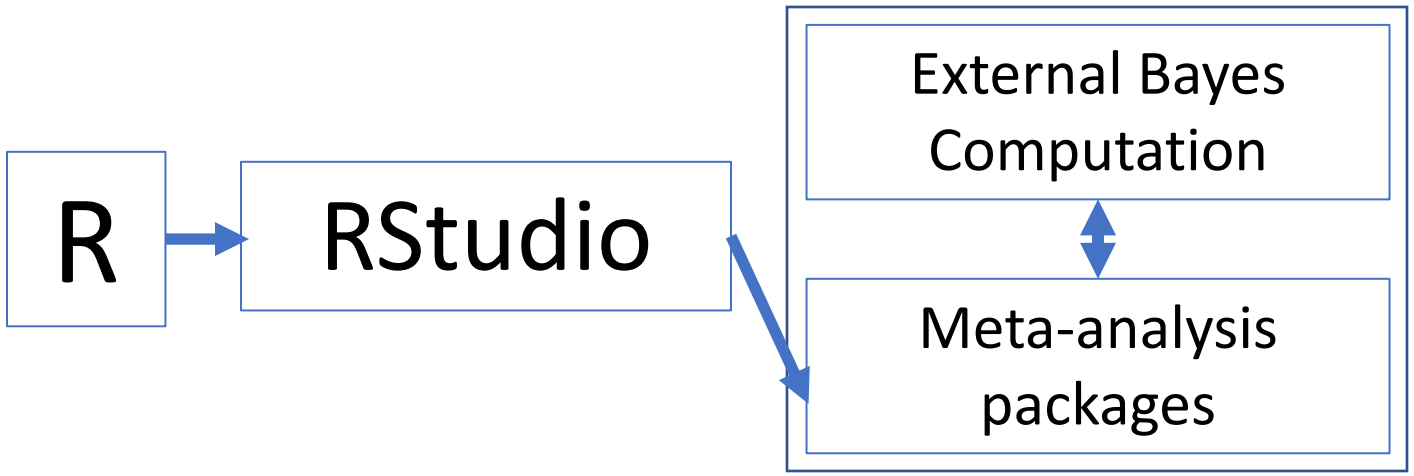
Recap: With an Automation lens

R

I did meta-analysis with S-plus / R in the 1990s/early 2000s

- Programmed myself “from scratch”, no packages for meta-analysis available

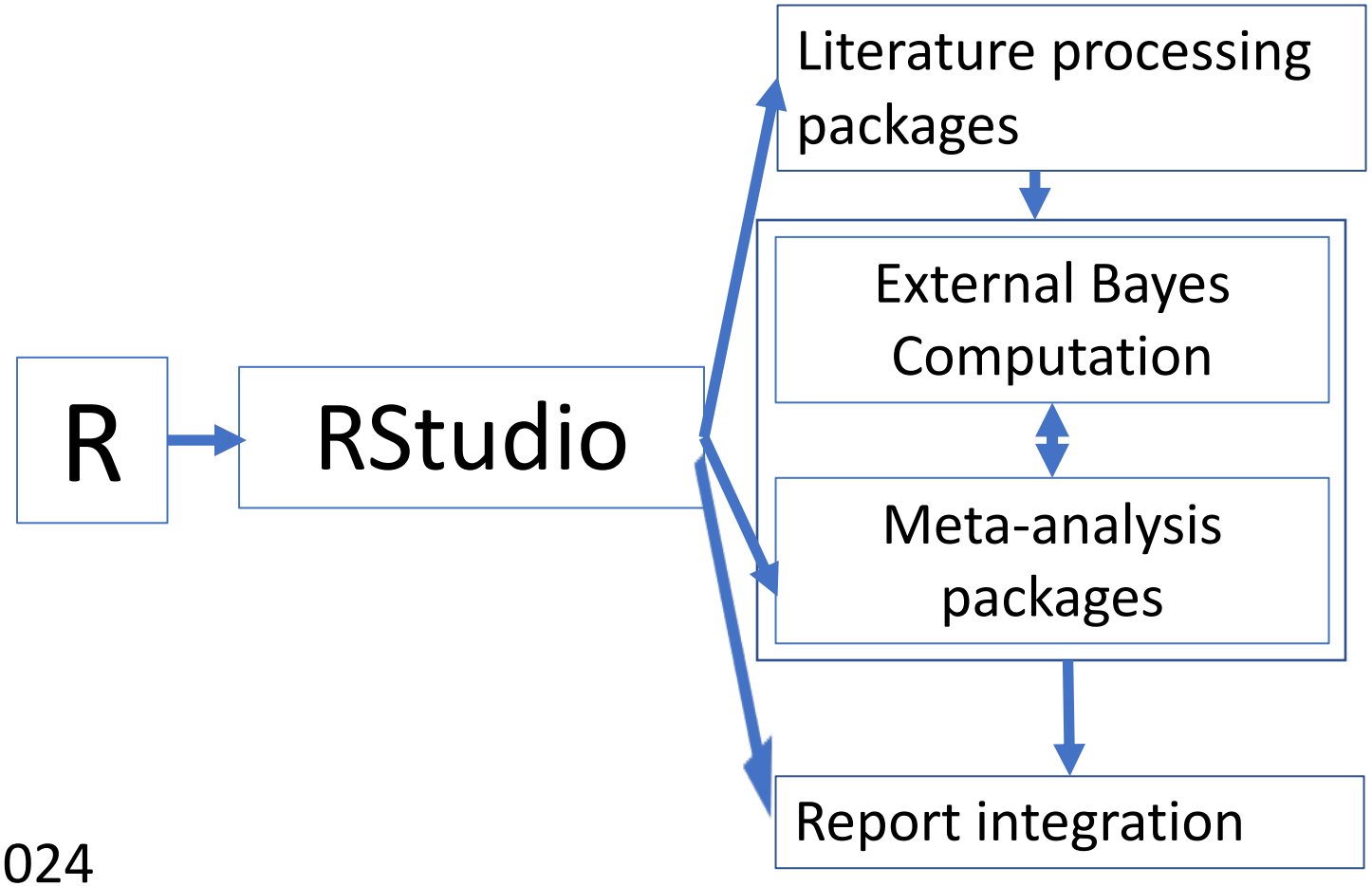
Recap: With an Automation lens



By 2010s

- Good meta-analysis / network meta-analysis capabilities via packages (including interface to Bayesian computation software)

Recap: With an Automation lens



2024

- Report writing integration fully realised
- Packages for literature processing emerging

{Shiny} – adding user interactivity

- Made by posit (https://www.rstudio.com/products/shiny/)
  - “Elegant and powerful web framework for building web applications using R.”
  - “Shiny helps you turn your analyses into interactive web applications without requiring HTML, CSS, or JavaScript knowledge”
  - Uses R in the background (run on the WebServer)

*** Alex show example app ****

How can {Shiny} be used for systematic reviews?

- Use 1 : Could be used to publish review report or supplement with interactivity to assist reader / offer information not possible in published version.
  - E.g. “How would the results of meta-analysis change if I omit study X from the analysis?”

- Use 2: Provide tools for the systematic reviewer with a bespoke interface
  - Can be used without the need to learn (or install) R at all!!

Example - Use 1 Interactive reporting

- Interactive REFerence Flow (I-REFF) diagram
  - Linked to the literature screening data, resulting in a simplified process for updating the diagram.
  - I-REFF diagrams enhance transparency and traceability by not only summarizing the records in the review but also allowing viewers to follow specific records throughout the review process.
  - Walker, V.R., Lemeris, C.R., Magnuson, K. *et al.* I-REFF diagrams: enhancing transparency in systematic review through interactive reference flow diagrams. *Syst Rev* **13**, 33 (2024). https://doi.org/10.1186/s13643-023-02420-0
  - https://public.tableau.com/app/profile/ntp.visuals/viz/GEN-11InteractivePRISMAExample/Dashboard1

**** Alex to Demo ****

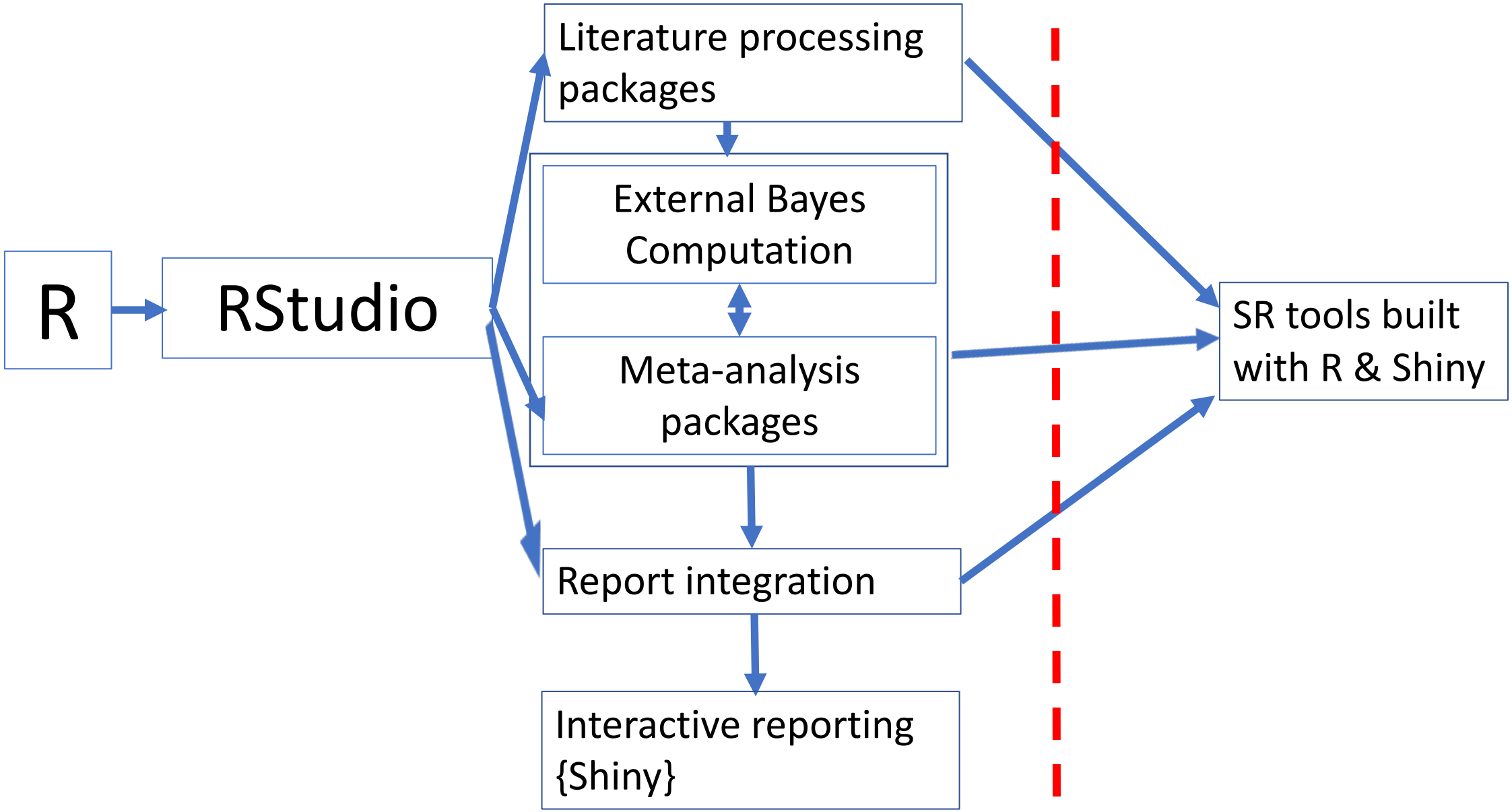
Example: Use 2 R-package in Shiny app

PRISMA2020 – Shiny package with app for producing Prisma flow diagrams for SR

- https://estech.shinyapps.io/prisma_flowdiagram/
- Also available as a package for use in R

*** Alex to Demo ****

Recap: With an Automation lens



CRSU apps for meta-analysis

- Complex Review Support Unit initial funding 2015-2023
- “The CRSU will focus on providing timely and appropriate support for the delivery of complex reviews that are funded and/or supported by NIHR.”
- Quickly discovered lack of software for the non-statistic expert systematic reviewer was a limiting factor
- Apps developed in response to this need
- We plan to use the apps for ESG work
  - We hope other ESG groups will find them useful too

App Principles

- Developed using R and {shiny} (with JAGS and STAN for Bayesian analysis)
- Where possible utilise existing R packages
- Free to use and open source
- Point and click interface
- Built in example datasets
- Do not replace statisticians
- Provide methods for sensitivity analysis
- Emphasis on visualization
- Export plots of publication quality

Relative Treatment Effects

- MetaPairwise
  - Pairwise meta-analysis
- MetaImpact
  - Designing studies to contribute to meta-analyses
- MetaInsight
  - Network meta-analysis (NMA)
- MetaCNMA 

  - Component network meta-analysis (CNMA)

- MetaInsightCOVID
  - Feasibility study for living NMA

Diagnostic Test Accuracy

- MetaDTA
  - Frequentist meta-analysis
- MetaBayesDTA
  - Bayesian meta-analysis

- DTAPrimer
  - Introduction to DTA

https://www.gla.ac.uk/research/az/evidencesynthesis/

**** Alex to Demo ****

Future Plans For The CRSU Apps

- Add report generation with associated underlying code to analysis apps
  - •Adds transparency / reproducibility
  - •Allow user to tweak / extend analysis beyond what is possible in the apps in R
- Embed apps in SR-Accelerator (https://sr-accelerator.com/#/)
- Make MetaInsight compatible with CINeMA app (quality assess NMA) (https://cinema.ispm.unibe.ch/)
- We always welcome feedback and suggestions for future developments!
  - All apps are open source and we would encourage and support those interested in extending the apps

References for CRSU apps:

1. Cerullo, E., Sutton, A.J., Jones, H.E. et al. **MetaBayesDTA: codeless Bayesian meta-analysis of test accuracy, with or without a gold standard.** *BMC Med Res Methodol* (2023); 23, 127 https://doi.org/10.1186/s12874-023-01910-y
2. Freeman SC, Kerby CR, Patel A, Cooper NJ, Quinn T, Sutton AJ. **Development of an interactive web-based tool to conduct and interrogate meta-analysis of diagnostic test accuracy studies: MetaDTA**. *BMC Medical Research Methodology* (2019); **19**: 81 https://doi.org/10.1186/s12874-019-0724-x
3. Nevill CR, Cooper NJ, Sutton AJ. **A multifaceted graphical display, including treatment ranking, was developed to aid interpretation of network meta-analysis.** J Clin Epidemiol. 2023 May;157:83-91. doi: 10.1016/j.jclinepi.2023.02.016. Epub 2023 Mar 3. PMID: 36870376.
4. Owen, RK, Bradbury, N, Xin, Y, Cooper, N, Sutton, A. **MetaInsight: An interactive web-based tool for analyzing, interrogating, and visualizing network meta-analyses using R-shiny and netmeta.** *Res Syn Meth*. 2019; 10: 569– 581.
5. Patel A, Cooper NJ, Freeman SC, Sutton AJ. **Graphical enhancements to summary receiver operating characteristic plots to facilitate the analysis and reporting of meta-analysis of diagnostic test accuracy data**. *Research Synthesis Methods* (2021); 12: 34-44. https://doi.org/10.1002/jrsm.1439
6. Xin Y, Nevill CR, Nevill J, Gray E, Cooper NJ, Bradbury N, Sutton AJ. **Feasibility study for interactive reporting of network meta-analysis: experiences from the development of the MetaInsight COVID-19 app for stakeholder exploration, re-analysis and sensitivity analysis from living systematic reviews.** *BMC Med Res Methodol*. 2022:22 (*article number 26*) https://doi.org/10.1186/s12874-022-01507-x

Conclusion

- R environment evolved a lot over previous 25 years and shows few signs of slowing down
- It has much to offer those conducting systematic reviews
  - Especially for meta-analysis
- Advent of {Shiny} means R power potentially available to the non R user
  - Apps becoming available with the systematic reviewer in mind
- Hopefully these slides provide jumping off places for those who want to explore further