Table 1. Selected Strengths and Weaknesses of Various Study Designs, along with Examples of Studies with Effects on Policy or Practice.

Data Source	Strengths	Weaknesses	Examples of Effects on Policy or Practice
Randomized, controlled trials	Can identify causal relationships Can reduce bias and confounding Can determine efficacy: can establish definitively which treatment methods are superior	Potential for validity to be limited to study population, with limited relevance to actual conditions Potential for surrogate markers, if used, to not correlate with outcome of interest Resource-intensive with regard to costs: high costs may lead to designs with inadequate sample size Resource-intensive with regard to time: completion may not occur until after introduction of new products or treatment methods, so that trials are not studying what is used in actual clinical practice Impractical for urgent situations and certain conditions (e.g., rare diseases) May not account for effects beyond study population (i.e., effects on persons not participating in the trial, such as spread of infection to others)	Trials have defined the cardiovascular benefits of lowering low-density lipoprotein cholesterol and of lowering blood pressure in various patient populations[75-77] Trials have established and continue to refine tuberculosis treatment regimens used globally[32,33]
Meta-analyses, systematic reviews, decision analyses	Can broaden capacity to test hypotheses and detect patterns and effects Allow for pooled results that can potentially yield more robust estimates Can adjust for underlying study rigor and sample size Do not require additional new data collection	Potential for invalid conclusions from the combination of different data sources; validity limited by quality of underlying studies and different methods of measuring the same outcome among studies; potential for false sense of precision Because many hypotheses can easily be tested, potential exists for introduction of systematic bias through selective publication of positive findings Limited availability of valid studies to analyze for some topics	Studies have evaluated factors associated with stroke, myocardial infarction, and death among patients with carotid artery stents[78] Studies have assessed effects of cholesterol-lowering medications and patient selection for this treatment[79,80] Studies have analyzed different approaches for prevention of cancer (e.g., among women with *BRCA1* or *BRCA2* mutations), for prevention of colon cancer, and for treatment of prostate cancer[81-83]
Prospective cohort studies	Establish temporal relationship Can evaluate a range of outcomes Can evaluate rare exposures Allow for nested studies	Inefficient for studying rare diseases Resource-intensive, since most cohorts must be followed for many years Potential for nonrepresentative study populations (e.g., persons who are less mobile) resulting from losses to follow-up	Identification of risk factors for breast and colon cancer, cardiovascular disease, hip fracture, eye disease, and decreased cognitive function (Nurses' Health Study) led to changes in screening, prevention, and treatment[84] Identification of risk of cancer and death among patients infected with hepatitis C virus led to intensified efforts to establish and provide effective treatment[85]
Retrospective cohort studies	Establish temporal relationship Can evaluate a range of outcomes associated with a given exposure Can evaluate rare exposures Allow for nested studies Can be conducted rapidly	Inefficient for studying rare diseases Resource-intensive (with regard to costs and time) Potential for difficulties in correcting for recall and other forms of bias and for confounding	Assessment of prognosis and treatment in different types of cancer led to better treatment protocols[86] Assessment of survivors of childhood cancer led to recognition of increased risk of post-treatment cardiac complications, enabling better clinical care[87]
Case–control studies	Efficient for studying rare outcomes and potential associated exposures Can be conducted rapidly and generally at low cost Can rapidly yield information with implications for action	Potential for varying quality of exposure assessment data May be more prone to bias than cohort studies because of selection bias and other study effects No information about rates of disease or temporal trends	Identification of risk factors for the sudden infant death syndrome (SIDS) led to intervention programs that have greatly reduced infant mortality[9] Determination of common exposures has led to identification of sources of infection and recalls of contaminated food[88] Identification of association between oropharyngeal cancer and human papillomavirus infection has led to new prevention efforts[89]

Table 1. (Continued.)

Data Source	Strengths	Weaknesses	Examples of Effects on Policy or Practice
Cross-sectional studies	Provide snapshot of exposure and outcome Can help generate hypotheses Can be conducted rapidly	Difficult to attribute causality Difficult to control for confounding	Evaluation of association between sodium intake and blood pressure, along with other evidence, has provided support for policy interventions aimed at reducing sodium consumption[46,48] Evaluation of deep venous thrombosis in hospitals led to the identification of a low rate of use of appropriate preventive measures and to improved practices[90]
Ecologic studies	Provide population-level vs. individual-level data Can document outcomes of natural experiments Can be conducted rapidly	Potential for invalid conclusions from noncausal associations because of residual confounding (ecologic fallacy) Potential for data that are not standardized or comparable	Vaccine-effectiveness studies have led to changes in immunization recommendations, increasing the proportion of people protected[29] Analysis of mortality in heat waves resulted in practical recommendations to mitigate weather-related effects[91]
Pragmatic trials and large observational studies	Potential for high generalizability Can be conducted at relatively low cost Potential to emulate real-world experience in application of findings, increasing external validity	Potential for varying quality of data Potential for adoption of some interventions by control group, biasing results toward a null result Potential for increased likelihood of invalid results because of a lack of standardization of assessment, treatment, and adherence Potential for loss to follow-up to affect interpretation of results	Study comparing treatments for type 2 diabetes was 20 times larger and had much longer follow-up than previous randomized, controlled trials, resulting in clear evidence for clinical decision making[63] and fewer patients being treated with a sulfonylurea, a drug class not previously known to be associated with increased mortality Trial provided evidence that task sharing among nurses and other health workers did not reduce quality of care for patients with human immunodeficiency virus infection[92]
Program-based evidence	May provide definitive evidence of efficacy in real-world conditions	Without control community, may not be possible to determine causality Potential for control community to adopt some of the interventions, biasing results toward a null result	New Zealand Back to Sleep campaign provided definitive evidence that advice given to parents about having babies sleep in a supine position could prompt actions that would reduce the incidence of SIDS,[9] leading to global programs that have greatly reduced infant mortality Implementation of public health measures such as tobacco taxes, smoke-free laws, and educational campaigns have documented efficacy in ways that would not have been possible or definitive otherwise and has led to widespread implementation of tobacco-control measures that save millions of lives[93]
Case reports and series	Can provide inexpensive, detailed assessments Useful for evaluation of rare diseases, identification of rare events Can lead to reasonable conclusions about relative benefit of different treatments for rare diseases	Limited ability to draw definitive conclusions because of the lack of a comparison group Selection bias (e.g., patients with rapid resolution or rapid progression to death may be underrepresented)	Identification of the acquired immunodeficiency syndrome and other newly recognized conditions (e.g., Zika virus–associated microcephaly and newly identified drug-resistant organisms or mechanisms) has accelerated improvements in detection, treatment, and prevention of these conditions[94,95] Highly effective treatments have been identified for conditions that otherwise had poor prognoses (e.g., penicillin as a broad-spectrum antibiotic)[96]
Registries	Determine efficacy in real life Can provide useful data for rare diseases Can help assess quality of care Can provide results rapidly	Difficult or impossible to control for confounding and bias	Studies have documented and improved quality of care and determined the most effective treatment of patients undergoing dialysis, reducing the incidence of preventable complications and deaths[97] Studies have determined predictors of survival in pulmonary arterial hypertension, enabling more informed treatment choices[98]