#### An Example, to Fix Ideas

Example (Krnjajić, Kottas, Draper [KKD] 2008): In-home geriatric assessment (IHGA). In an experiment conducted in the 1980s (Hendriksen et al. 1984), 572 elderly people, representative of  $\mathcal{P} = \{$ all non-institutionalized elderly people in Denmark $\}$ , were randomized, 287 to a control ( $\mathcal{C}$ ) group (who received standard health care) and 285 to a treatment ( $\mathcal{T}$ ) group (who received standard care plus IHGA: a kind of preventive medicine in which each person's medical and social needs were assessed and acted upon individually).

One **important outcome** was the **number of hospitalizations** during the **two-year** life of the study:

	Number of Hospitalizations						
Group	0	1		k	n	Mean	SD
Control	n <sub>C0</sub>	n <sub>C1</sub>		n <sub>Ck</sub>	$n_C = 287$	ӯс	sc
Treatment	$n_{T0}$	$n_{T1}$		$n_{Tk}$	$n_T = 285$	$ar{y}_{\mathcal{T}}$	$s_T$

Let  $\mu_C$  and  $\mu_T$  be the **mean hospitalization rates** (per two years) in  $\mathcal P$  under the C and T conditions, respectively.

Here are **four statistical questions** that **arose** from **this study**:

## The Four Principal Statistical Activities

 $Q_1$ : Was the mean number of hospitalizations per two years in the IHGA group smaller than that in control by an amount that was large in practical terms?  $\left[\begin{array}{c} \mathbf{description} & \text{involving} \end{array} \left(\begin{array}{c} \overline{y}_T - \overline{y}_C \\ \overline{y}_C \end{array}\right)\right]$ 

Q<sub>2</sub>: Did IHGA reduce the mean number of hospitalizations per two years by an amount that was large in statistical terms?

$$\left[ \text{inference about } \left( \frac{\mu_T - \mu_C}{\mu_C} \right) \right]$$

Q<sub>3</sub>: On the **basis** of **this study**, how **accurately** can You **predict** the **total decrease** in **hospitalizations** over a period of *N* years if **IHGA** were **implemented throughout Denmark?** [prediction]

 $Q_4$ : On the **basis** of **this study**, is the **decision** to **implement IHGA** throughout Denmark **optimal** from a **cost-benefit** point of view? [decision-making]

These questions encompass almost all of the discipline of statistics: describing a data set D, generalizing outward inferentially from D, predicting new data  $D^*$ , and helping people make decisions in the presence of uncertainty (I include sampling/experimental design under decision-making; omitted: data quality assurance (QA), ...).

# Quantification of Uncertainty

Quantification of uncertainty: Classical, frequentist and Bayesian definitions of probability.

 $\textit{Case study} \colon \textbf{Diagnostic screening} \ \text{for} \ \textbf{HIV}$ 

Widespread **screening for HIV** has been proposed by **some people** in **some countries** (e.g., the **U.S.** in 1985).

Two blood tests that screen for HIV are widely available: *ELISA*, which is relatively inexpensive (roughly \$20) and fairly accurate; and *Western Blot (WB)*, which is considerably more accurate but costs quite a bit more (about \$100).

A new patient comes to You, a physician, with symptoms that suggest he may be HIV positive (Good, 1950: You = a generic person wishing to reason sensibly in the presence of uncertainty).

#### Questions

 Is it appropriate to use the language of probability to quantify Your uncertainty about the true/false proposition

 $A = \{ \text{this patient is HIV positive} \}$ ?

#### **Definition of Statistics**

#### Questions

- If so, what kinds of probability are appropriate, and how would You assess P(A) in each case?
  - What **strategy** (e.g., *ELISA*, *WB*, both?) should You **employ** to **decrease Your uncertainty** about *A*?

If You decide to run a screening test, how should Your uncertainty be updated in light of the test results?

Statistics might be defined as the study of uncertainty: how to measure it well, and how to make good choices in the face of it, and probability as the part of mathematics devoted to the quantification of uncertainty.

The systematic study of probability is fairly recent in the history of ideas, dating back to about 1650 (e.g., Hacking, 1975).

# Definitions of Probability

In the last **350** years **three main ways to define probability** have arisen (e.g., Oakes, 1990):

- Classical (Pascale, Fermat): Enumerate the elemental outcomes (EOs) in a way that makes them equipossible on, e.g., symmetry grounds, and compute  $P_C(A)$  = the ratio of  $n_A$  =(number of EOs favorable to A) to n =(total number of EOs).
- Frequentist (Venn, von Mises): Restrict attention to attributes A of events: phenomena that are inherently repeatable under "identical" conditions; define  $P_F(A) =$  the limiting value of the relative frequency with which A occurs as the number of repetitions  $\to \infty$ .
- Personal, or "Subjective," or Bayesian: two equivalent definitions:
- (Bayes, de Finetti) Imagine **betting with someone** about the **truth** of the **proposition** A, and **ask Yourself** what **odds**  $O_{You}$  (in favor of A) You would need to **give or receive** in order that You **judge** the bet to befair; then (for You)  $P_{B:You}(A) = \frac{O_{You}}{(1+O_{You})}$ .

#### Pros and Cons

— (Laplace, RT Cox, Jaynes)  $P_{B:You}(A)$  is a numerical measure of the weight of evidence in favor of proposition A, based on Your current information, and required to satisfy a set of reasonable axioms to achieve internal logical consistency.

Other approaches not covered here include logical (Keynes, Jeffreys, Carnap) and fiducial (Fisher) probability.

Each of these **probability definitions** has general **advantages** and **disadvantages**:

- Classical: Plus: Simple, when applicable (e.g., idealized coin-tossing, drawing colored balls from urns, ... ).
- Classical: Minus: The only way to define "equipossible" without a circular appeal to probability is through the principle of insufficient reason You judge EOs equipossible if You have no grounds (empirical, logical, or symmetrical) for favoring one over another but this leads to paradoxes (e.g., assertion of equal uncertainty on an infinite set is not invariant to the choice of scale).

## Pros and Cons (continued)

- Frequentist: Plus: Mathematics relatively tractable.
- Frequentist: Minus: Only applies to inherently repeatable events, e.g., (as of November 2011)  $P_F$  (Barack Obama will be re-elected in 2012) is (strictly speaking) undefined.
  - Bayesian: Plus: All forms of uncertainty are in principle quantifiable with this approach.
- Bayesian: Minus: There's no guarantee that the answer You get by querying Yourself about betting odds or weight of evidence will retrospectively be seen by You or others as "good" (but how should the quality of an uncertainty assessment itself be assessed?).

#### Application to HIV Screening

$$P(A) = P($$
this patient is HIV-positive $) = ?$ 

Data are available from medical journals on prevalence of HIV-positivity in various subsets of  $\mathcal{P} = \{ \text{all humans} \}$  (e.g., it's higher in gay people, and lower in older people).

### Probability Modeling is Judgmental

All three probabilistic approaches require You to use Your judgment to identify the recognizable subpopulation  $\mathcal{P}_{\mathsf{this}\;\mathsf{patient}}$  (Fisher, 1956; Draper et al., 1993): this is

the largest subset to which this patient belongs for which the HIV prevalence differs from that in the rest of  $\mathcal P$  by an amount You judge as large enough to matter in a practical sense.

Within  $\mathcal{P}_{\text{this patient}}$  You regard HIV prevalence as close enough to constant that the differences are not worth bothering over, but the differences between HIV prevalence in  $\mathcal{P}_{\text{this patient}}$  and its complement matter to You.

Here  $\mathcal{P}_{\text{this patient}}$  might consist of **everybody** who **matches** this patient on (e.g.) **gender**, **age** (category, e.g., 25–29), and **sexual orientation**.

NB This is a modeling choice based on judgment; different reasonable people might make different choices; thus probability modeling in the real world is inherently subjective (see page 15 below for more details).

#### The Three Probability Definitions in Practice

As a **classicist** You would then (a) use this **definition** to **establish equipossibility** within  $\mathcal{P}_{\text{this patient}}$ , (b) **count**  $n_A =$  (the number of HIV-positive people in  $\mathcal{P}_{\text{this patient}}$ ) and n = (the total number of people in  $\mathcal{P}_{\text{this patient}}$ ), and (c) compute  $P_C(A) = \frac{n_A}{n}$ .

As a frequentist You would (a) equate P(A) to P(a) person chosen at random with replacement (i.e., independent identically distributed (IID) sampling) from  $\mathcal{P}_{\text{this patient}}$  is HIV-positive), (b) imagine repeating this random sampling indefinitely, and (c) conclude that the limiting value of the relative frequency of HIV-positivity in these repetitions would also be  $P_F(A) = \frac{n_A}{n}$ .

 $\overline{\text{NB}}$  Strictly speaking You're not allowed in the frequentist approach to talk about P(this patient is HIV-positive): either he is or he isn't; in the frequentist paradigm, You can only talk about the process of sampling people like him from  $\mathcal{P}_{\text{this patient}}$ .

As a Bayesian, with the information given here You would regard this patient as exchangeable (de Finetti, e.g., 1964, 1974/5) with all other patients in  $\mathcal{P}_{\text{this patient}}$  — meaning informally that You judge Yourself

#### Exchangeability and Coherence

equally uncertain about HIV-positivity for all the patients in this set — and this judgment, together with the axioms of coherence, would also yield  $P_{B:You}(A) = \frac{n_A}{n}$  (although I've not yet said why this is so).

Exchangeability and coherence will be defined and explored in more detail in what follows.

Note that with the same information base the three approaches in this case have led to the same answer, although the meaning of that answer depends on the approach, e.g., frequentist probability describes the process of observing a repeatable event, whereas Bayesian probability is an attempt to quantify Your uncertainty about something, repeatable or not.

The classical and frequentist approaches have sometimes been called "objective", whereas the Bayesian approach is clearly subjective, and — since objectivity sounds like a good goal in science — this has sometimes been used as a claim that the classical and frequentist approaches are superior.

## "Objectivity" and Subjectivity

I'd argue, however, that in interesting applied problems of realistic complexity, the judgment of equivalence or similarity (equipossibility, IID, exchangeability) that's central to all three theories makes them all subjective in practice.

Imagine, for example, that You were given data on HIV prevalence in a large group of people, along with many variables (possible predictors) that might or might not be relevant to identifying the recognizable subpopulations.

You and other reasonable people working independently might well differ in your judgments on which of these predictors are relevant (and how they should be used in making the prediction), and the result could easily be noticeable variation in the estimates of P(HIV positive) obtained by You and the other analysts, even if everyone attempts to use "objective" methods to arrive at these judgments (there are many such methods, and they don't always lead to the same conclusions).

Thus the assessment of complicated probabilities is inherently subjective — there are "judgment calls" built into probabilistic and statistical analysis.

# "Objectivity" and Subjectivity (continued)

With this in mind attention in all three approaches should evidently shift away from trying to achieve "objectivity" toward two things:

- (1) the **explicit statement** of the **assumptions** and **judgments made** on the way to Your **probability assessments**, so that **other people** may consider their **plausibility**, and
  - (2) sensitivity analyses exploring the mapping from assumptions to conclusions.
- (To a Bayesian, saying that  $P_B(A)$  is objective just means that lots of people more or less agree on its value.)

Suppose that, with **this patient's values** of **relevant demographic variables**, the **prevalence** of HIV **estimated** from the **medical literature**, P(A) = P(he's HIV-positive), in his recognizable subpopulation is about  $\frac{1}{100} = \textbf{0.01}$ .

To improve this estimate by gathering data specific to this patient, You decide to draw some blood and get a result from *ELISA*.

## Sequential Learning; Bayes's Theorem

Suppose the **test** comes back **positive** — what's Your **updated** P(A)?

Bayesian probability has that name because of the simple updating rule attributed to Thomas Bayes (1763), who was the first person to define conditional probability and make calculations with it:

Bayes's Theorem for propositions: 
$$P(A|D) = \frac{P(A)P(D|A)}{P(D)}$$
 (1)

In the **usual application** of this, A is an **unknown quantity** (such as the **truth value** of some **proposition**) and D stands for some **data** relevant to Your **uncertainty** about A:

$$P(\text{unknown}|\text{data}) = \frac{P(\text{unknown}) P(\text{data}|\text{unknown})}{\text{normalizing constant}}$$

$$posterior = c \cdot prior \cdot likelihood \qquad (2)$$

The terms prior and posterior emphasize the sequential nature of the learning process — P(unknown) was Your uncertainty assessment before the data arrived; this is updated multiplicatively on the probability scale by the likelihood P(data|unknown), and renormalized

#### Bayes's Theorem in Odds Form

so that **total probability** remains 1 — but **in general** the **prior** is a **quantification** of **all information** about the **unknown external** to the **present data set**.

Writing the **Theorem** both for A and (not A) and **combining** gives a (perhaps even **more**) **useful** version: **Bayes's Theorem in Odds Form:** 

Another name for the Bayes factor is the likelihood ratio, since this factor measures the relative plausibility of the data given A and (not A).

Applying this to the HIV example requires additional information about *ELISA* obtained by screening the blood of people with known HIV status:

**sensitivity** = 
$$P(ELISA \text{ positive}|HIV \text{ positive})$$
 and (4)  
**specificity** =  $P(ELISA \text{ negative}|HIV \text{ negative})$ .

## Sensitivity and Specificity

In practice, in 1985 *ELISA*'s **operating characteristics** were (or at least seemed) **rather good** — **sensitivity** about **0.95**, **specificity** about **0.98** — so You might well **expect** that P(this patient HIV positive|ELISA|positive) would be **close to 1**.

Here the **updating** produces a **surprising result** (if you've never **seen this sort of thing** before): the **Bayes factor** comes out

$$B = \frac{\text{sensitivity}}{1 - \text{specificity}} = \frac{0.95}{0.02} = 47.5,$$
 (5)

which sounds like strong evidence that this patient is HIV positive, but the prior odds are quite a bit stronger the other way  $(\frac{P(A)}{1-P(A)}=99$  to 1 against HIV), leading to posterior odds of  $\frac{99}{47.5} \doteq 2.08$  against HIV, i.e.,  $P(\text{HIV positive}|\text{data}) = \frac{1}{1+\text{odds}} = \frac{95}{293} \doteq \textbf{0.32}$  (!).

The reason for this is that *ELISA* was designed to have a vastly better false negative rate —  $P(\text{HIV positive}|\ ELISA\ \text{negative}) = \frac{5}{9707} \doteq 0.00052 \doteq 1 \text{ in } 1941$  — than false positive rate —  $P(\text{HIV negative}|\ ELISA\ \text{positive}) = \frac{198}{293} \doteq 0.68 \doteq 2 \text{ in } 3.$ 

## Inference and Decision-Making

This in turn is because ELISA's developers judged that it's far worse to tell somebody who's HIV positive that they're not than the other way around (reasonable for using ELISA for, e.g., blood bank screening).

This **false positive rate** would make widespread screening for HIV based only on *ELISA* a **truly bad idea**.

Formalizing the consequences of the two types of error in diagnostic screening would require quantifying misclassification costs, which shifts the focus from (scientific) inference (the acquisition of knowledge for its own sake: Is this patient really HIV-positive?) to decision-making (putting that knowledge to work to make a choice, e.g.: What use of ELISA and Western Blot would yield the optimal screening strategy?).

Axiomatic approaches to rational decision-making date back to Ramsay (1926), with von Neumann and Morgenstern (1944) and Savage (1954) also making major contributions.

# Bayesian Decision Theory

The **ingredients** of a **general decision problem** (e.g., Bernardo and Smith, 1994) **include** 

- A set  $\{a_i, i \in I\}$  of available **actions**, one of which You will **choose**;
  - For each action  $a_i$ , a set  $\{E_j, j \in J\}$  of uncertain outcomes describing what will happen if You choose action  $a_i$ ;
- A set  $\{c_j, j \in J\}$  of **consequences** corresponding to the **outcomes**  $\{E_j, j \in J\}$ ; and
- A preference relation  $\leq$ , expressing Your preferences between pairs of available actions ( $a_1 \leq a_2$  means " $a_1$  is not preferred by You to  $a_2$ ").

**Define** 
$$a_1 \sim a_2$$
 (" $a_1$  and  $a_2$  are **equivalent**" to You) iff  $a_1 \leq a_2$  and  $a_2 \leq a_1$ .

This preference relation induces a qualitative ordering of the uncertain outcomes ( $E \le F$  means "E is not more likely than F"), but within this framework further assumptions — the coherence axioms — are needed to ensure that Your actions are internally consistent.

## Decision-Theory Axioms

**Informally** (see Bernardo and Smith, 1994, for the **formalism**) these are:

- An axiom insisting that You be willing to express preferences between simple dichotomized possible actions ({a, not a});
- A transitivity axiom in which (for all actions  $a, a_1, a_2, a_3$ )  $a \le a$ , and if  $a_1 \le a_2$  and  $a_2 \le a_3$  then  $a_1 \le a_3$ ; and
- An axiom based on the sure-thing principle: if, in two situations, no matter how the first comes out the corresponding outcome in the second is preferable, then You should prefer the second situation overall.

This puts ≤ on a **sound footing** for **qualitative uncertainty assessment**, but **does not yet imply** how to **quantify** — it's like being able to **say** that **one thing weighs less than another** but not to say **by how much**.

To go further requires a fourth assumption, analogous to the existence of a set of reference standards (e.g., an official kg weight, half-kg, and so on) and the ability to make arbitrarily precise comparisons with these standards:

### Utility; Implications

 An axiom guaranteeing that for each outcome E there exists a standard outcome S (e.g., "idealized coin lands heads") such that E ~ S.

This framework implies the existence and uniqueness of a (personal) probability  $P_{B:You}$  (abbreviated P), mapping from outcomes E to [0,1] and corresponding to the judgments in Your definition of  $\leq$ , and a

utility function  $U_{You}$  (abbreviated U; large values preferred, without loss of generality), mapping from consequences c to  $\Re$  and quantifying Your preferences.

This has all been rather **abstract**; **three concrete results** arising from this **framework** may make its **implications clearer**:

• Bayes's original definition of personal probability is helpful in thinking about how to quantify uncertainty.

**Supposing** that **consequences** are **monetary** (e.g., **US\$**), to say that  $P_{B:You}(E) = p$  for some **uncertain outcome** E whose **truth value** will be **known** in the **future** is to say that You're **indifferent** between

#### **Dutch Book**

- (a) receiving  $(p \cdot m)$  for sure (for some hypothetical (and reasonably small) amount of money m and (b) betting with someone in such a way that You'll get m if E turns out to be true and nothing if not (You can use this to estimate  $P_{B:You}(E)$ ).
- Any coherent set of probability judgments must satisfy the standard axioms and theorems of a finitely additive probability:

$$-0 \le P(E) \le 1 \text{ and } P(E^c) = 1 - P(E);$$

- $P(E_1 \text{ or } \dots \text{ or } E_J) = \sum_{j \in J} P(E_j)$  for any finite collection  $\{E_j, j \in J\}$  of disjoint outcomes;
- $P(E \text{ and } F) = P(E) \cdot P(F)$  for any two **independent outcomes** (informally, E and F are **independent** if Your **uncertainty judgments** involving **one of them** are **unaffected** by **information** about the **other**); and
- Conditional probability has a natural definition in this setup, corresponding to the **updating** of Your **uncertainty** about E in light of E, and with this definition  $P(E|F) = \frac{P(E \text{ and } F)}{P(F)}$ .

#### Maximization of Expected Utility

Otherwise (de Finetti, 1964) someone betting with You on the basis of Your probability judgments can make Dutch book against you, i.e., get You to agree to a series of bets that are guaranteed to lose You money.

Thus coherent Bayesian probability obeys the same laws as with the classical and frequentist approaches (apart from a technical issue about finite versus countable additivity).

Nothing so far has said clearly what choice to make in a decision problem if You wish to avoid incoherence.

If the outcomes were certain You'd evidently choose the action that maximizes Your utility function, but since they're not the best action must involve weighing both Your probabilities for the uncertain outcomes and the utilities You place on their consequences.

It's a direct implication of the framework here that the form this weighing should take is simple and clear:

#### **HIV Case Study**

#### Maximization of Expected Utility (MEU)

Given Your probability and utility judgments, Your decision-making is coherent iff for each action  $a_i$ , with associated uncertain outcomes  $\{E_j, j \in J\}$  and consequences  $\{c_j, j \in J\}$ , You compute the expected utility  $\mathsf{EU}_i = \sum_{j \in J} U(c_j) P(E_j)$  and choose the action that maximizes  $\{\mathsf{EU}_i, i \in I\}$ .

Example: HIV screening. As a simplified version of this problem consider choosing between two actions:

- $a_1$ : Obtain *ELISA* results at a cost of  $c_1 = $20$ ; if **positive**, conclude this patient is **HIV**+, if **negative**, conclude **HIV**-.
- $a_2$ : Same as  $a_1$  except if *ELISA* comes out **positive**, obtain *Western Blot (WB)* results at an additional cost of  $c_2 = \$100$ ; if *WB* is **positive** conclude **HIV**+, if **negative** conclude **HIV**-.

With action  $a_1$  the **probabilities**, **uncertain outcomes**, and **utilities** are as follows:

## HIV Case Study (continued)

	True HIV	ELISA	
Probability	Status	Status	Utility
.0095	+	+	$-c_1$
.0005	+	_	$-c_1-L_1$
.0198	_	+	$-c_1-L_{II}$
.9702	_	_	$-c_1$

Here  $L_{I}$  and  $L_{II}$  are the **false negative (false positive)** monetary losses suffered by this patient if he really is HIV+ (HIV-) but *ELISA* says he is HIV- (HIV+).

The **expected utility** with **action**  $a_1$  is thus

$$EU_1 = .0095(-c_1) + .0005(-c_1 - L_1) + ... + .9702(-c_1)$$
  
=  $-(c_1 + .0005L_1 + .0198L_{II})$ . (6)

The **corresponding table** for **action**  $a_2$  is:

## HIV Case Study (continued)

	True HIV	ELISA	WB	
Probability	Status	Status	Status	Utility
.00945	+	+	+	$-c_1 - c_2$
.00005	+	+	_	$-c_1-c_2-L_1$
.00004	+	_	+	$-c_1-L_1$
.00046	+	_	_	$-c_1-L_1$
.00010	_	+	+	$-c_1-c_2-L_{II}$
.01970	_	+	_	$-c_1 - c_2$
.00095	_	_	+	$-c_1$
.96925	_	_	_	$-c_1$

These **probabilities arise** from *WB*'s **design** (the **goal** was to have **about the same false negative rate** as *ELISA* and a **much lower false positive rate** (about 0.1), leading to a **slightly worse sensitivity** (0.949) but **much improved specificity** (0.999)).

The expected utility with action a2 comes out

$$EU_2 = .00945(-c_1 - c_2) + ... + .9604(-c_1)$$
  
=  $-(c_1 + .0293c_2 + .00055L_1 + .0001L_{II})$ . (7)

By **MEU** You should **prefer**  $a_2$  to  $a_1$  iff  $EU_2 > EU_1$ , i.e., iff

#### **HIV Case Study**

$$|.0197L_{II} - .00005L_{I} - .0293c_{2} > 0.$$

Thus  $a_2$  becomes **more desirable** as the **loss** suffered with a **false positive** (negative) increases (decreases), and less desirable as WB's cost increases, all of which makes good sense.

It's **interesting** to note that with a **modest value** for  $L_{II}$  (e.g., \$1,000), the **monetary advantage** from taking action  $a_2$  is **quite small**, even with a **realistically huge value** for  $L_I$  (e.g., \$100,000, which leads to an **edge** for  $a_2$  of **only about** \$12).

This is due to the extremely low false negative rate for both tests —  $L_1$  would have to be over \$335,000 for  $a_1$  to dominate!

Overall conclusion: for realistic values of  $L_1$  and  $L_{11}$  the adaptive strategy  $a_2$  is **better**.

We'll see many more examples of maximizing expected utility later in this short course.

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