# Personalized prognosis & decision: An example study on the conversion from Mild Cognitive Impairment to Alzheimer's Disease

**P.G.L. Porta Mana** [1,2,*]**, I. Rye** [3]**, A. Vik** [1,2]**, M. Kociński** [2,4]**, A. Lundervold** [2,4]**,**

**A. J. Lundervold** [3]**, A. S. Lundervold** [1,2]

[1]*Department of Computer Science, Electrical Engineering and Mathematical Sciences, Western Norway University of Applied Sciences, Bergen, Norway*
[2]*Mohn Medical Imaging and Visualization Centre (MMIV), Department of Radiology, Haukeland University Hospital, Bergen, Norway*
[3]*Department of Biological and Medical Psychology, University of Bergen, Norway*
[4]*Department of Biomedicine, University of Bergen, Norway*

Correspondence*:
P.G.L Porta Mana, HVL, Inndalsveien 28, 5063 Bergen
pgl@portamana.org

## ABSTRACT

Patients with Mild Cognitive Impairment have an increased risk of a trajectory toward Alzheimer's Disease. Early identification of patients with a high risk of Alzheimer's Disease is essential to provide treatment before the disease is well-established in the brain. great importance to study how well different kinds of predictors allow us to prognose a trajectory from Mild Cognitive Impairment towards Alzheimer's Disease in an individual patient.

But more is needed for a personalized approach to prognosis, prevention, and treatment, than just the obvious requirement that prognoses be as best as they can be for each patient. Several situational elements that can be different from patient to patient must be accounted for:

- the *kinds* of clinical data and evidence available for prognosis;
- the *outcomes* of the same kind of clinical data and evidence;
- the kinds of treatment or prevention strategies available, owing to different additional medical factors such as physical disabilities, different attitudes toward life, different family networks and possibilities of familial support, different economic means;
- the advantages and disadvantages, benefits and costs of the same kinds of treatment or prevention strategies; the patient has a major role in the quantification of such benefits and costs;
- finally, the initial evaluation by the clinician – which often relies on too subtle clues (family history, regional history, previous case experience) to be considered as measurable data.

Statistical decision theory is the normative quantification framework that takes into account these fundamental differences. Medicine has the distinction of having been one of the first fields to adopt this framework, exemplified in brilliant old and new textbooks on clinical decision-making.

Clinical decision-making makes allowance for these differences among patients through two requirements. First, the quantification of prognostic evidence on one side, and of benefits and costs of treatments and prevention strategies on the other, must be clearly separated and handled in a modular way. Two patients can have the same prognostic evidence and yet very different prevention options. Second, the quantification of independent prognostic evidence ought to be in the form of *likelihoods about the health condition* (or equivalently of likelihood ratios, in a binary case), that is, of the probabilities of the observed test outcomes given the hypothesized health conditions. Likelihoods from independent clinical tests and predictors can then be combined with a simple multiplication; for one patient, we could have three kinds of predictor available; for another, we could have five. The clinician's pre-test assessment is included in the form of a probability. These patient-dependent probabilities are combined with the patient-dependent costs and benefits of treatment or prevention to arrive at the best course of action for that patient. The main result underlying statistical decision theory is that decision-making *must* take this particular mathematical form in order to be optimal and logically consistent.

The present work investigates the prognostic power of a set of neuropsychological and Magnetic Resonance Imaging examinations, demographic data, and genetic information about Apolipoprotein-E4The present work investigates the prognostic power of a set of neuropsychological and Magnetic Resonance Imaging examinations, demographic data, and genetic information about Apolipoprotein-E4 (APOE) status, for the prediction of the onset of Alzheimer's Disease in patients defined as mildly cognitively impaired at a baseline examination. The longitudinal data used come from the ADNI database.

(APOE) status, for the prediction of the onset of Alzheimer's disease in patients defined as mildly cognitively impaired at a baseline examination. The longitudinal data used come from the ADNI database.

The prognostic power of these predictors is quantified in the form of a combined likelihood for the onset of Alzheimer's disease. As a hypothetical example application of personalized clinical decision making, three patient cases are considered where a clinician starts with prognostic uncertainties, possibly coming from other tests, of 50%/50%, 25%/75%, 75%/25%. It is shown how these pre-test probabilities are changed by the predictors. 🔧 update this

🔧 rewrite following This quantification also allows us to rank the relative prognostic power of the predictors. It is found that several neuropsychological examinations have the highest prognostic power, much higher than the genetic and imaging-derived predictors included in the present set.

Several additional advantages of this quantification framework are also exemplified and discussed in the present work:

- missing data are automatically handled, and results having partial data are not discarded; this quantification, therefore, also accounts for patient-dependent availability of *non-independent* predictors;
- no modelling assumptions (e.g., linearity, gaussianity, functional dependence) are made;

- the prognostic power obtained is intrinsic to the predictors, that is, it is a bound for *any* prognostic algorithm;
- variability ranges of the results owing to the finite size of the sample data are automatically quantified.
- the values obtained, being probabilities, are more easily interpretable than scores of various kinds.

**Keywords: Clinical decision making, Utility theory, Probability theory, Artificial Intelligence, Machine Learning, Base-rate fallacy**

## 1 EACH PATIENT IS UNIQUE

Meet Olivia, Ariel, Bianca, Curtis.[1] These four persons don't know each other, but they have something in common: they all suffer from a mild form of cognitive impairment, and are afraid that their impairment will turn into Alzheimer's Disease within a couple of years. In fact, this is why they recently underwent some clinical analyses and cognitive tests. Today they received the results of their analyses. From these results, available clinical statistical data, and other relevant information, their clinician will assess their risk of developing Alzheimer. The clinician and each patient will then decide among a set of possible preventive treatments.

Besides this shared condition and worry, these patients have other things in common – but also some differences. Let's take Olivia as reference and list the similarities and difference between her and the other three:

- Olivia and Ariel turn out to have exactly identical clinical results and age. They would also get similar benefits from the available preventive-treatment options. Ariel, however, comes from a different geographical region from Olivia, where the conversion rate from Mild Cognitive Impairment to Alzheimer is lower: about 30%, whereas in Olivia's it is around 45% (Petersen et al., 1999) Moreover there is no history of Alzheimer's Disease in Ariel's family.
- Olivia and Bianca also have exactly the same clinical results and age. They come from the same geographical region and have very similar family histories. In fact we shall see that they have the same probability of developing Alzheimer's disease. Bianca, however, suffers from several allergies and additional clinical conditions that would render some of the preventive options less beneficial to her.
- Olivia and Curtis have different clinical results – in particular, Olivia has the risky Apolipoprotein-E4 (APOE4) allele (Liu et al., 2013) whereas Curtis hasn't – and age, Olivia being more than 20 years older than Curtis. But they otherwise come from the same geographical region, have very similar family histories, and would get similar benefits from the preventive options.

We can categorize these differences as "difference in auxiliary information" (Olivia and Ariel), "difference in preventive benefits" (Olivia and Bianca), "difference in clinical factors" (Olivia and Curtis). Figure 1 summarizes the similarity and differences between Olivia and the other three patients. Table 1 reports the clinical results and demographic data common to Olivia, Ariel, Bianca, as well as those of Curtis 🔧 need to explain the variates and refer to (Rye et al., 2022).

Considering the similarities and differences among these patients, which treatments are optimal and should prescribed to them?

---

[1] Fictive characters; any reference to real persons is purely coincidental

**Figure 1.** ✎ draft, needs better font sizes

| Patient | Age | Sex | HC · $10^{-3}$ | APOE4 | ANART | CFT | GDS | RAVLT-im | RAVLT-del | RAVLT-rec | TMTA | TMTB |
|---|---|---|---|---|---|---|---|---|---|---|---|---|
| *Olivia, Ariel, Bianca* | 83.5 | F | 2.77 | Y | 14 | 18 | 0 | 29 | 12 | 3 | 126.5 | 117.0 |
| *Curtis* | 61.5 | M | 4.17 | N | 6 | 13 | 1 | 16 | 2 | 0 | 24.8 | 83.4 |

**Table 1.** 🔧 Clinical results & demographic data

Our main purpose in the present work is to illustrate, using the four fictitious patients above as example, how this clinical decision-making problem can today be solved methodically, exactly, and at low computational cost, when the available prognostic clinical information involves one-dimensional or categorical variates such as those listed in table 1. The solution method integrates available clinical statistical data with each new patient's unique combination of clinical results, auxiliary information, and treatment benefits.

In our example we shall find that – despite the many factors in common among our four patients, even despite the identical clinical results for Olivia, Ariel, Bianca, and despite the identical probability of conversion for Olivia and Bianca – *the optimal treatment option for each patient is different from those for the other three*. This result exemplifies the importance of differences among patients with regard to clinical results, auxiliary information, or preventive benefits.

The method used is none other than decision theory, the combination of probability theory and utility theory (von Neumann and Morgenstern, 1955; Raiffa and Schlaifer, 2000; Raiffa, 1970; Berger, 1985; Jaynes, 2003). Medicine has the distinction of having been one of the first fields to adopt it (Ledley and Lusted, 1959), with old and new brilliant textbooks (Weinstein and Fineberg, 1980; Sox et al., 2013; Hunink et al., 2014) that explain and exemplify its application.

Decision theory is also the normative foundation for the construction of an Artificial Intelligence agent capable of rational inference and decision making (Russell and Norvig, 2022, ch. IV; Jaynes, 2003, chs 1–2). The present method can therefore be seen as the application of an *ideal machine-learning algorithm*. "Ideal" in the sense of being free from approximations, special modelling assumptions, and limitations in its informational output; not in the sense of being impracticable. Another important point of the present work, indeed, is to show that *for some kinds of dataset* such ideal machine-learning algorithm is a reality. It is preferable to popular algorithms such as neural networks, random forests, support-vector machines, which are unsuited to clinical decision-making problems owing to their output limitations. We discuss this matter further in §🔧 ***.

✎ Add other advantages of this exact approach:

- it does not make assumptions, besides natural assumption of smoothness of full-population frequency distribution
- can be used with partially missing clinical data

- can be used with binary or continuous predictands
- it tells us the maximum predictive power of the predictors
- it quantifies how prediction could change if we had more sample data
- it can be applied on-the-fly to each new patient

and goals, results, and some synopsis

The inferential and decision-making steps are summarized in table 2.

---

**Table 2.** Inferential and decision-making steps. Steps in **boldface** represent patient-dependent, personalized steps that cannot be obtained from the learning dataset

1. Infer the full-population frequencies of predictors and predictand, using available datasets.

2. **Assess in respect of which variates the present patient can be considered as belonging to the same population underlying the learning dataset.**

3. **Assess the prior probability of the predictand for the present patient.** This step allows us (a) to consider additional clinical information outside of the dataset's variates, and available for the present patient only; (b) to correct for mismatches between the dataset's underlying population and the patient's one.

4. Calculate the *likelihood* of the predictand for a specific patient, given the patient's predictor values. Combine this likelihood with the prior from step 3, to obtain the final probability for the predictand, for the present patient.

5. **Assess the clinical courses of action available for the present patient, together their benefits and costs.** This step is fundamentally patient-dependent and is the one open to most variability from patient to patient.

6. Choose the course of action having maximal expected benefit for the present patient, given the benefits assessed in step 5 and the final probability assessed in step 4.

---

## 2 ✏ PRACTICAL EXAMPLE

🧩 It may be optimal to present the steps in reverse order: the last one explains the goal, and makes clear why the preceding steps are necessary.

### 2.1 Learning

In the learning stage we infer the statistical relationships of a large population of which our future patients can be considered members, at least in some respects. Such relationships will help us in our prognoses. The basic idea is intuitive. If a patient can be considered a member of this population, and if we knew the joint frequencies of all possible combinations of predictor and predictand values in such population – and knew nothing else – then we would say that the probability for the patient to have particular values is equal

**Figure 2.** ✏ Upper-left: Sample data. Upper-right: candidate frequency distribution that fits the data and does not look unnatural. Lower-left: candidate distribution that might look natural but doesn't fit the sample data. Lower-right: candidate distribution that fits the data very well but looks unnatural.

to the population frequency. Pure symmetry considerations lead to this intuitive result (de Finetti, 1930; Dawid, 2013; Bernardo and Smith, 2000, §§ 4.2–4.3).

But it must be emphasized, and it is essential for our method, that it is *not* necessary (and is seldom true) that a future patient be considered as a member of such a population *in all respects*. A patient can be considered a member only *conditionally* on particular variate values. We shall discuss this point with an example in § 2.2.

If the full statistics of such a population were known, our task would just be to "enumerate" rather than to "learn". Learning comes into play because the full population is not known: we only have a sample from it.

The most we can do is therefore to assign a probability to each possible frequency distribution for the full population. The probability of a specific "candidate" frequency distribution is intuitively determined by two factors: (a) how well it fits the sample data, (b) how biologically or physically reasonable it is. Figure 2 show a fictitious sample data and various candidate frequency distributions ✏ ....

✏ Some more intuition and details about the maths, principles, and characteristics (Dunson and Bhattacharya, 2011; Rossi, 2014; Rasmussen, 1999).

**Figure 3.** ✏ Examples of a-priori probable candidates of frequency distribution for a variate such as AVDEL30MIN_neuro or AVDELTOT_neuro

The core of our method is the computation of the probabilities of all possible frequency distributions for the full population. From it we obtain the joint probability distribution $\mathrm{p}(X, Y, Z, \dots)$ for all variates $X, Y, Z, \dots$ available in the dataset.

This is the maximal amount of information that can be extract from our dataset. From it we can indeed quickly calculate any quantity typically outputted by specific or approximate algorithms. For example:

- *Conditional probability, "discriminative" algorithms:* if we are interested in the probability of $Z$ given $X, Y$, we calculate $\mathrm{p}(Z \mid X, Y) := \mathrm{p}(X, Y, Z) / \sum_Z \mathrm{p}(X, Y, Z)$.

- *Conditional probability, "generative" algorithms:* if we are interested in the probability of $X, Y$ given $Z$, we calculate $\mathrm{p}(X, Y \mid Z) := \mathrm{p}(X, Y, Z) / \sum_{X,Y} \mathrm{p}(X, Y, Z)$.

- *Regression or classification:* if we are interested in the average value of $Z$ given $X, Y$, we calculate $\mathrm{E}(Z \mid X, Y) := \sum_Z Z \, \mathrm{p}(Z \mid X, Y)$. The "noise" around this average value is moreover given by $\mathrm{p}(Z - \mathrm{E} \mid X, Y)$.

- *Functional regression:* if $Z$ turns out to be a function $f$ of $X, Y$, then the probability will be a delta distribution: $\mathrm{p}(Z \mid X, Y) = \delta[Z - f(X, Y)]$. The present ideal machine-learning algorithm thus always recovers a functional relationship if there is one, including its noise distribution.

We will see that no one of these quantities can be used alone to solve our clinical decision problem for all future patients.

The present method moreover has some further advantages and yields additional useful information:

- *Discrete or continuous variates:* the variate to be prognosed can be not only binary or discrete, as in the present case, but also continuous.

- *Partially missing data:* data having missing values for some variates can be fully used, both in the learning dataset and in the prognostic results of new patients.

- *Maximal predictive power of the variates:* from the probability distribution $\mathrm{p}(X, Y, Z, \dots)$ we can calculate the mutual information between any two sets of variates, for example between $Z$ and $\{X, Y\}$. This quantity tells us what is the maximal predictive power – which can be measured by accuracy or other metrics – from one set to the other that can be achieved by any inference algorithm (MacKay, 2005; Good and Toulmin, 1968; Cover and Thomas, 2006). Functional dependence is included as a special case; for example, a binary variate $Z$ is a function of $\{X, Y\}$ if and only if their mutual information [2] equals $1\,\mathrm{Sh}$.

- *Variability owing to limited sample size:* we can calculate how much any of the quantities listed so far – from average values to mutual information – could change if more sample data were added to our dataset.

For readers with an interest in machine learning and artificial intelligence, we briefly discuss the drawbacks of some popular inference algorithms with respect to the present ideal algorithm.

*Neural networks and gaussian processes* are based on the assumption that there is a functional relationship from predictors to predictand, possibly contaminated by a little noise, typically assumed gaussian. This is a very strong assumption, quite unrealistic for many kinds of variables considered in medicine. It can only be justified in the presence of informationally very rich predictors such as images. In our case the mutual information between predictors and the conversion variate is $0.14\,\mathrm{Sh}$, to be compared with $1\,\mathrm{Sh}$, if conversion were a function of the predictors, and with $0\,\mathrm{Sh}$, if conversion were completely unpredictable. See § ✎ \*\*\* for further details. An additional deficiency of neural networks is that they do not yield any probabilities, even if there are many efforts to render such an output possible (Pearce et al., 2020; Osband et al., 2021; Back and Keith, 2019). Such an advance, however, would still not solve the final deficiency of neural networks and gaussian processes: they try to infer the predictand from the predictors but cannot be used for the reverse inference.

*Random forests* also assume a functional relationship from predictors to predictand. This assumptions is mitigated when the predictand is a discrete variate; in this case a random forest can output an agreement score from its constituent decision trees. This score can give an idea of the underlying uncertainty, but it is not a probability,[3] and therefore cannot be used in the decision-making stage, see § 2.6. It is possible to transform this score into a proper probability (Dyrland et al., 2022), but this possibility does not solve the final deficiency of random forests: like neural networks, they try to infer the predictand from the predictors but cannot be used for the reverse inference.

*Parametric models and machine-learning algorithms* such as logistic or linear regression, support-vector machines, or generalized linear models make even stronger assumptions than neural networks and random forests. They assume specific functional shapes or frequency distributions. Their use may be justified when we are extremely sure – for instance thanks to underlying physical or biological knowledge – of the validity of their assumptions; or when the computational resources are extremely scarce. But it is otherwise unnecessary to be hampered by their restrictive and often unrealistic assumptions.

An important common deficiency of most inference algorithms mentioned above is that their inference only goes from predictors to predictands. In the next two sections we shall see that this precludes – or makes

---

[2] The "shannon" (Sh) is a measurement unit of information, as specified by the ISO (International Organization for Standardization) (2008).

[3] This score is sometimes called a "non-calibrated probability", which is akin to calling a shape a "non-round circle".

---

much riskier – the prognostic use of the learning dataset for patients belonging to different populations, such as Ariel.

### 2.1.1 Random forests

## 2.2 Population assessment

Let's clarify this with an example. In our dataset we observe a value $\mathsf{GDS} = 1$ with a frequency of 32% across all patients. Among the patients who later converted to Alzheimer's Disease, the frequency is 36%; whereas among those who remained with a stable Mild Cognitive Impairment, the frequency is 28%. Given a new patient, if we knew that

(Lindley and Novick, 1981; Sprenger and Weinberger, 2021; Bar-Hillel, 1980)

## 2.3 Prior probability

(Lindley and Novick, 1981; Sprenger and Weinberger, 2021; Bar-Hillel, 1980)

## 2.4 Likelihood and posterior probability

(Lindley and Novick, 1981; Sprenger and Weinberger, 2021; Bar-Hillel, 1980)

## 2.5 Benefit assessments

(Sox et al., 2013; Hunink et al., 2014)

## 2.6 Maximization of expected benefit

(Lindley, 1982)

— Luca, old pieces of text —

Personalized diagnosis, prognosis, treatment, and prevention strategies must make allowance for several fundamental differences among patients:

- the *kinds* of clinical data and evidence available for diagnosis or prognosis can be different;
- the *values* of the same kind of clinical data and evidence can be different;
- the kinds of treatment or prevention options can be different;
- the advantages and disadvantages, benefits and costs of the same kinds of treatment or prevention can be different;
- finally, the evaluation of the clinician – which often relies on too subtle clues (family history, regional history, case experience) to be considered as measurable data – can be different.

Is there really a methodological framework that can take all these differences into account? Yes, there is, and Medicine has the distinction of having been one of the first fields to adopt it (Ledley and Lusted, 1959): Statistical Decision Theory. Its application in Medicine is explained and exemplified in several, brilliant, old and new textbooks (Weinstein and Fineberg, 1980; Sox et al., 2013; Hunink et al., 2014). This theory has mathematical and logical foundations and its principles constitute indeed the foundations for the definition and realization of Artificial Intelligence (Russell and Norvig, 2022) 🔧

The basics of clinical decision making 🔧 ..basics: each piece of evidence contributes with a likelihood or odds; they combine together and together with the clinician's pre-data evaluation. Then they are combined with the different benefits/costs of treatments or prevention strategies to find the optimal one. Decision trees can be necessary (but don't change this framework). Costs & benefits are evaluated by clinician & patient together.

$$
\overbrace{\mathrm{p}(\text{health condition} \mid \text{results of all tests, prior info})}^{\textit{post-test probability}} \propto
$$

$$
\overbrace{\mathrm{p}(\text{health condition} \mid \text{prior info})}^{\textit{pre-test probability by clinician}} \times
$$

$$
\textit{likelihoods of tests} \begin{cases} \mathrm{p}(\text{result of 1st test} \mid \text{health condition, prior info}) \times \\ \mathrm{p}(\text{result of 2nd test} \mid \text{health condition, prior info}) \times \\ \qquad\qquad\qquad\qquad\qquad\qquad \ldots \end{cases} \quad (1)
$$

# 3 ARTICLE TYPES

For requirements for a specific article type please refer to the Article Types on any Frontiers journal page. Please also refer to Author Guidelines for further information on how to organize your manuscript in the required sections or their equivalents for your field

# 4 MANUSCRIPT FORMATTING

## 4.1 Heading Levels

## 4.2 Level 2

### 4.2.1 Level 3

#### *4.2.1.1 Level 4*

##### *4.2.1.1.1 Level 5*

## 4.3 Equations

Equations should be inserted in editable format from the equation editor.

$$\sum x + y = Z \tag{2}$$

## 4.4 Figures

Frontiers requires figures to be submitted individually, in the same order as they are referred to in the manuscript. Figures will then be automatically embedded at the bottom of the submitted manuscript. Kindly ensure that each table and figure is mentioned in the text and in numerical order. Figures must be of sufficient resolution for publication see here for examples and minimum requirements. Figures which are not according to the guidelines will cause substantial delay during the production process. Please see here for full figure guidelines. Cite figures with subfigures as figure **??** and **??**.

### 4.4.1 Permission to Reuse and Copyright

Figures, tables, and images will be published under a Creative Commons CC-BY licence and permission must be obtained for use of copyrighted material from other sources (including re-published/adapted/modified/partial figures and images from the internet). It is the responsibility of the authors to acquire the licenses, to follow any citation instructions requested by third-party rights holders, and cover any supplementary charges.

## 4.5 Tables

Tables should be inserted at the end of the manuscript. Please build your table directly in LaTeX.Tables provided as jpeg/tiff files will not be accepted. Please note that very large tables (covering several pages) cannot be included in the final PDF for reasons of space. These tables will be published as Supplementary Material on the online article page at the time of acceptance. The author will be notified during the typesetting of the final article if this is the case.

# 5 NOMENCLATURE

## 5.1 Resource Identification Initiative

To take part in the Resource Identification Initiative, please use the corresponding catalog number and RRID in your current manuscript. For more information about the project and for steps on how to search for an RRID, please click here.

## 5.2 Life Science Identifiers

Life Science Identifiers (LSIDs) for ZOOBANK registered names or nomenclatural acts should be listed in the manuscript before the keywords. For more information on LSIDs please see Inclusion of Zoological Nomenclature section of the guidelines.

# 6 ADDITIONAL REQUIREMENTS

For additional requirements for specific article types and further information please refer to Author Guidelines.

## CONFLICT OF INTEREST STATEMENT

The authors declare that the research was conducted in the absence of any commercial or financial relationships that could be construed as a potential conflict of interest.

## AUTHOR CONTRIBUTIONS

The authors were too immersed in the development of the present work to keep a detailed record of who did what.

## FUNDING

Details of all funding sources should be provided, including grant numbers if applicable. Please ensure to add all necessary funding information, as after publication this is no longer possible.

## ACKNOWLEDGMENTS

This is a short text to acknowledge the contributions of specific colleagues, institutions, or agencies that aided the efforts of the authors.

## SUPPLEMENTAL DATA

Supplementary Material should be uploaded separately on submission, if there are Supplementary Figures, please include the caption in the same file as the figure. LaTeX Supplementary Material templates can be found in the Frontiers LaTeX folder.

## DATA AVAILABILITY STATEMENT

The datasets [GENERATED/ANALYZED] for this study can be found in the [NAME OF REPOSITORY] [LINK].

## REFERENCES

Back, A. and Keith, W. (2019). *Bayesian Neural Networks for Financial Asset Forecasting*. Master's thesis, KTH Royal Institute of Technology, Stockholm. `http://urn.kb.se/resolve?urn=urn:nbn:se:kth:diva-252562`

Bar-Hillel, M. (1980). The base-rate fallacy in probability judgments. *Acta Psychol.* 44, 211–233. DOI: `10.1016/0001-6918(80)90046-3`

Barnard, G. A., Bernardo, J. M., Dinges, H., Shafer, G., Silverman, B. W., Smith, C. A. B., et al. (1982). Discussion of paper by D. V. Lindley. Reply. *Int. Stat. Rev.* 50, 11–26. DOI:`10.2307/1402449`, DOI:`10.2307/1402450`, DOI:`10.2307/1402451`, DOI:`10.2307/1402452`, DOI:`10.2307/1402453`, DOI:`10.2307/1402454`, DOI:`10.2307/1402455`, DOI:`10.2307/1402456`. See (Lindley, 1982)

Berger, J. O. (1985). *Statistical Decision Theory and Bayesian Analysis.* Springer series in statistics (New York: Springer), 2 edn. DOI:`10.1007/978-1-4757-4286-2`. First publ. 1980

Bernardo, J. M., Bayarri, M. J., Berger, J. O., Dawid, A. P., Heckerman, D., Smith, A. F. M., et al. (eds.) (2011). *Bayesian Statistics 9* (Oxford: Oxford University Press). DOI:`10.1093/acprof:oso/9780199694587.001.0001`

Bernardo, J.-M. and Smith, A. F. (2000). *Bayesian Theory.* Wiley series in probability and mathematical statistics (New York: Wiley), repr. edn. DOI:`10.1002/9780470316870`. First publ. 1994

Cifarelli, D. M. and Regazzini, E. (1979). Considerazioni generali sull'impostazione bayesiana di problemi non parametrici. Le medie associative nel contesto del processo aleatorio di Dirichlet. *Riv. mat. sci. econ. soc.* 2, 39–52, 95–111

Cover, T. M. and Thomas, J. A. (2006). *Elements of Information Theory* (Hoboken, USA: Wiley), 2 edn. DOI:`10.1002/0471200611`. First publ. 1991

Damien, P., Dellaportas, P., Polson, N. G., and Stephens, D. A. (eds.) (2013). *Bayesian Theory and Applications* (Oxford: Oxford University Press). DOI:`10.1093/acprof:oso/9780199695607.001.0001`

Dawid, A. P. (2013). Exchangeability and its ramifications. In (Damien et al., 2013), chap. ch. 2. 19–29. DOI:`10.1093/acprof:oso/9780199695607.003.0002`

de Finetti, B. (1929). Funzione caratteristica di un fenomeno aleatorio. In *Atti del Congresso Internazionale dei Matematici:*, ed. S. Pincherle (Bologna: Zanichelli), vol. 6. 179–190. `https://www.mathunion.org/icm/proceedings`, `http://www.brunodefinetti.it/Opere.htm`. Transl. in (Cifarelli and Regazzini, 1979). See also (de Finetti, 1930)

de Finetti, B. (1930). Funzione caratteristica di un fenomeno aleatorio. *Atti Accad. Lincei: Sc. Fis. Mat. Nat.* IV, 86–133. `http://www.brunodefinetti.it/Opere.htm`. Summary in (de Finetti, 1929)

Dunson, D. B. and Bhattacharya, A. (2011). Nonparametric Bayes regression and classification through mixtures of product kernels. In (Bernardo et al., 2011). 145–158. DOI:`10.1093/acprof:oso/9780199694587.003.0005`, older version at `https://www.researchgate.net/publication/228447342_Nonparametric_Bayes_Regression_and_Classification_Through_Mixtures_of_Product_Kernels`

[Dataset] Dyrland, K., Lundervold, A. S., and Porta Mana, P. G. L. (2022). A probability transducer and decision-theoretic augmentation for machine-learning classifiers. Open Science Framework DOI:`10.31219/osf.io/vct9y`

Good, I. J. and Toulmin, G. H. (1968). Coding theorems and weight of evidence. *IMA J. Appl. Math.* 4, 94–105. DOI:`10.1093/imamat/4.1.94`

Hunink, M. G. M., Weinstein, M. C., Wittenberg, E., Drummond, M. F., Pliskin, J. S., Wong, J. B., et al. (2014). *Decision Making in Health and Medicine: Integrating Evidence and Values* (Cambridge: Cambridge University Press), 2 edn. DOI:`10.1017/CBO9781139506779`. First publ. 2001

ISO (International Organization for Standardization) (2008). *ISO 80000-13:2008: Quantities and units 13: Information science and technology*. International Organization for Standardization, Geneva

Jaynes, E. T. (2003). *Probability Theory: The Logic of Science* (Cambridge: Cambridge University Press). Ed. by G. Larry Bretthorst. First publ. 1994. DOI:`10.1017/CBO9780511790423`, `https://archive.org/details/XQUHIUXHIQUHIQXUIHX2`, `http://www-biba.inrialpes.fr/Jaynes/prob.html`

Ledley, R. S. and Lusted, L. B. (1959). Reasoning foundations of medical diagnosis: Symbolic logic, probability, and value theory aid our understanding of how physicians reason. *Science* 130, 9—21. DOI:`10.1126/science.130.3366.9`

Lindley, D. V. (1982). Scoring rules and the inevitability of probability. *Int. Stat. Rev.* 50, 1–11. DOI:`10.2307/1402448`. See also discussion and reply in (Barnard et al., 1982)

Lindley, D. V. and Novick, M. R. (1981). The role of exchangeability in inference. *Ann. Stat.* 9, 45–58. DOI:`10.1214/aos/1176345331`

Liu, C.-C., Kanekiyo, T., Xu, H., and Bu, G. (2013). Apolipoprotein E and Alzheimer disease: risk, mechanisms and therapy. *Nat. Rev. Neurol.* 9, 106–118, 184. DOI:`10.1038/nrneurol.2012.263`, DOI:`10.1038/nrneurol.2013.32`

MacKay, D. J. C. (2005). *Information Theory, Inference, and Learning Algorithms* (Cambridge: Cambridge University Press), version 7.2 (4th pr.) edn. `https://www.inference.org.uk/itila/book.html`. First publ. 1995

[Dataset] Osband, I., Wen, Z., Asghari, M., Ibrahimi, M., Lu, X., and Van Roy, B. (2021). Epistemic neural networks. arXiv DOI:`10.48550/arXiv.2107.08924`

Pearce, T., Leibfried, F., Brintrup, A., Zaki, M., and Neely, A. (2020). Uncertainty in neural networks: Approximately Bayesian ensembling. *Proc. Mach. Learn. Res.* 108, 234–244

Petersen, R. C., Smith, G. E., Waring, S. C., Ivnik, R. J., Tangalos, E. G., and Kokmen, E. (1999). Mild cognitive impairment: Clinical characterization and outcome. *Arch. Neurol.* 56, 303–308, 760. DOI:`10.1001/archneur.56.3.303`, `https://jamanetwork.com/journals/jamaneurology/fullarticle/775068`

Raiffa, H. (1970). *Decision Analysis: Introductory Lectures on Choices under Uncertainty*. Behavioral science: quantitative methods (Reading, USA: Addison-Wesley), 2nd pr. edn. First publ. 1968

Raiffa, H. and Schlaifer, R. (2000). *Applied Statistical Decision Theory*. Wiley Classics Library (New York: Wiley), repr. edn. First publ. 1961

Rasmussen, C. E. (1999). The infinite Gaussian mixture model. *Adv. Neural Inf. Process. Syst. (NIPS)* 12, 554–560. `https://www.seas.harvard.edu/courses/cs281/papers/rasmussen-1999a.pdf`

Rossi, P. E. (2014). *Bayesian Non- and Semi-parametric Methods and Applications*. The Econometric and Tinbergen Institutes lectures (Princeton: Princeton University Press). DOI:`10.1515/9781400850303`

Russell, S. J. and Norvig, P. (2022). *Artificial Intelligence: A Modern Approach*. Pearson series in artificial intelligence (Harlow, UK: Pearson), fourth global ed. edn. `http://aima.cs.berkeley.edu/global-index.html`, `https://archive.org/details/artificial-intelligence-a-modern-approach-4th-edition`. First publ. 1995

Rye, I., Vik, A., Kocinski, M., Lundervold, A. S., and Lundervold, A. J. (2022). Predicting conversion to Alzheimer's disease in individuals with Mild Cognitive Impairment using clinically transferable features. *Sci. Rep.* 12, 15566. DOI:`10.1038/s41598-022-18805-5`

Sox, H. C., Higgins, M. C., and Owens, D. K. (2013). *Medical Decision Making* (New York: Wiley), 2 edn. DOI:`10.1002/9781118341544`. First publ. 1988

Sprenger, J. and Weinberger, N. (2021). Simpson's paradox. In *Stanford Encyclopedia of Philosophy*, ed. E. N. Zalta (Stanford: The Metaphysics Research Lab). `https://plato.stanford.edu/arc hives/sum2021/entries/paradox-simpson`

von Neumann, J. and Morgenstern, O. (1955). *Theory of Games and Economic Behavior* (Princeton: Princeton University Press), 3rd ed., 6th pr. edn. `https://archive.org/details/in.ernet .dli.2015.215284`. First publ. 1944

Weinstein, M. C. and Fineberg, H. V. (1980). *Clinical Decision Analysis* (Philadelphia: Saunders)