Evidentiary Distance and The Translation of Surrogate-Endpoint Evidence into Pharmaceutical Marketing Claims

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Abstract
Purpose: Pharmaceutical claims are often accurate at the level of the clinical trial endpoint yet are read by consumers as promises about living longer or feeling better. This paper theorises that translation problem and develops a regulatory-marketing framework linking evidence properties, claim design and consumer inference.
Design/methodology/approach: The paper is conceptual. It integrates four literature streams, covering surrogate endpoint validity and expedited approval, pharmaceutical promotion and consumer comprehension, marketing theory on information asymmetry, signalling, inference and disclosure, and international regulatory guidance. Synthesis is concept-centric and yields construct definitions, a framework and propositions rather than pooled evidence.
Findings: The framework introduces evidentiary distance, the separation between the clinical meaning an endpoint supports and the patient benefit a recipient can reasonably infer from a communication built on it. It is a property of the evidence-claim pair, not of the evidence alone. Six propositions link it to claim amplification, transparency calibration, consumer benefit inference and trust, moderated by framing, disclosure comprehensibility, literacy and disease severity.
Practical implications: Marketers and medical-legal-regulatory reviewers can assess evidentiary distance alongside literal claim accuracy, testing whether inferred benefit stays within the scope the endpoint supports. Regulators can judge disclosures by whether they correct inference rather than merely state facts.
Originality/value: The phenomenon has been observed in regulatory science and health communication but has not been given a marketing-theoretic account. The paper supplies that account, defines four constructs and sets out a measurement agenda.

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1. Introduction

A television advertisement for an oncology medicine states that the product stopped tumours from growing for longer than the comparator did. Every word can be true of the trial. What a viewer takes away is often something else, that the drug helps people live longer. Randomised experiments conducted by regulatory researchers found this pattern directly. Adults shown fictitious advertisements built on progression-free survival made significantly more errors about survival benefit than adults shown overall survival claims, and a plain sentence stating that survival benefit was not yet known improved the accuracy of their expectations (Sullivan *et al*., 2023). The distance between what the evidence established and what the audience concluded is a marketing problem, not only a regulatory one.

Surrogate endpoints make that distance structural. Tumour response, progression-free survival, viral load, cholesterol concentration and bone mineral density stand in for outcomes patients care about, on the assumption that movement in the marker will track movement in the outcome (Prentice, 1989; Biomarkers Definitions Working Group, 2001). That assumption is often only partly met. Trial-level associations between common oncology surrogates and survival are frequently weak or unreported (Prasad *et al*., 2015; Ciani *et al*., 2017), medicines approved on surrogates often show no later survival gain (Kim and Prasad, 2015; Gyawali *et al*., 2019), and confirmatory evidence after expedited approval can be slow, incomplete or absent in both the United States and Europe (Naci *et al*., 2017; Davis *et al*., 2017; Banzi *et al*., 2017; Vokinger *et al*., 2022). Regulators accept this trade-off deliberately, to shorten the time between a serious unmet need and an available treatment (Fleming, 2005; FDA, 2026; EMA, 2020). The trade-off is defensible. The communication consequences of it are the subject of this paper.

Medical and regulatory research has examined the evidentiary side of the problem in depth. It has assessed endpoint validity (Bikowski 2026), catalogued distorted reporting of trial results, known as spin (Chiu *et al*., 2017; Boutron *et al*., 2014), traced how distortion travels through press releases into news coverage (Yavchitz *et al*., 2012), and documented selective endpoint reporting in oncology advertising itself (Wayant *et al*., 2020). Patients and clinicians misunderstand progression-free survival even in clinical settings (Fallowfield *et al*., 2017; MacEwan *et al*., 2019; Sullivan *et al*., 2020). What this work has not done is explain the phenomenon in terms of how consumers process commercial messages.

Marketing research has the explanatory apparatus. It has long treated unequal access to product information as the defining condition of quality-uncertain markets (Akerlof, 1970; Nelson, 1970; Darby and Karni, 1973), has theorised how firms signal unobservable quality (Spence, 1973; Kirmani and Rao, 2000; Erdem and Swait, 1998; Connelly *et al*., 2011), has mapped the inferences consumers draw beyond what a message literally says (Hoch and Ha, 1986; Kardes *et al*., 2004), and has classified truthful claims that mislead by implication (Johar, 1995; Hastak and Mazis, 2011). Work in this journal has examined direct-to-consumer advertising, scepticism, endorsement and brand credibility in pharmaceutical settings (Mukherjee *et al*., 2013; Ju, 2017; Rollins *et al*., 2020; Bairrada *et al*., 2021), and the wider debate about whether promotion to the public informs or distorts demand is long-running (Woloshin *et al*., 2001; Mintzes, 2012). None of this work treats the clinical trial endpoint as the evidentiary input that constrains what a claim can honestly mean.

That is the gap this paper addresses, and it should be stated precisely. The phenomenon is empirically documented, mainly in oncology and mainly by regulatory-science teams. It is not theorised. No account exists of how the properties of endpoint evidence interact with the properties of a commercial message to produce a benefit inference that outruns the evidence, or of what that mismatch does to credibility when it is later disconfirmed.

The paper therefore asks four questions. How does the distance between a surrogate endpoint and a consumer-inferred clinical benefit affect the meaning of a pharmaceutical claim? Which communication features widen or narrow that distance? How do disclosure, source credibility and regulatory context shape trust when evidentiary uncertainty is communicated? And how can marketers communicate surrogate-endpoint evidence without converting a bounded finding into an implied broader promise?

Three contributions follow. First, the paper defines evidentiary distance and three related constructs, and distinguishes them from adjacent concepts already in use. Second, it brings regulatory evidence characteristics into marketing theory, treating the endpoint as an input to the signalling process rather than as background. Third, it converts the framework into six propositions and a measurement agenda that empirical researchers can test. Section 2 sets out the evidence problem, Section 3 describes the synthesis method, Section 4 builds the theoretical foundation, Section 5 defines the constructs, Section 6 presents the framework and propositions, and Sections 7 to 11 cover boundary conditions, implications and future research.

2. Surrogate Endpoints as A Marketing Evidence Problem

A surrogate endpoint is a measure intended to substitute for a clinical outcome and to predict it (Biomarkers Definitions Working Group, 2001). Its usefulness depends on whether treatment effects on the marker reliably predict treatment effects on the outcome, a condition that is demanding and often untested (Prentice, 1989; Fleming and DeMets, 1996). Surrogates vary widely in how well that condition is met. Some are well validated across a therapeutic area. Others are accepted as reasonably likely to predict benefit, which is the standard applied under expedited pathways (FDA, 2018, 2026). Others are used because they are measurable and early, with little evidence linking them to anything patients experience.

This variation matters commercially because it is invisible in the message. A claim built on a validated surrogate and a claim built on a poorly validated one can be worded identically. Both can pass a literal accuracy check. Neither carries a marker of how much clinical meaning sits behind it. The regulatory record contains the distinction, in approval documents, product information and endpoint guidance (FDA, 2018; EMA, 2024), but that record is not what consumers see.

Three features of the pharmaceutical setting make the resulting problem sharper than in most consumer categories. First, patients cannot verify treatment performance from their own experience in the way they can judge a meal or a hotel. For a preventive therapy, or for a therapy whose benefit is measured in months of survival, personal experience gives almost no diagnostic signal (Darby and Karni, 1973; Hoch and Ha, 1986). Second, the technical vocabulary of endpoints is not part of ordinary language. Terms such as response rate and progression-free survival are read through a lay frame in which any improvement implies feeling better and living longer (Sullivan *et al*., 2020; Fallowfield *et al*., 2017). Third, the decision is frequently made under distress, when motivation to find a favourable interpretation is high.

Evidence that consumers close this gap in the direction of hope is consistent. Advertisements often present efficacy in vague qualitative terms rather than quantified terms (O'Donoghue *et al*., 2014), consumers overestimate what regulatory approval certifies (O'Donoghue *et al*., 2016), and disclosure of accelerated approval status on manufacturer

websites has been limited (Sullivan *et al*., 2018). Content analyses of promotional material continue to find selective endpoint reporting and emotional framing that outruns the underlying data (Wayant *et al*., 2020; Applequist and Ball, 2018). The problem is not that surrogate endpoints are invalid. It is that the scope of what consumers infer can exceed the scope of what the evidence supports, and that nothing in an ordinary claim tells them where the boundary lies.

3. Approach to The Literature Synthesis

This is a conceptual paper and does not claim to be a systematic review. It uses a targeted integrative synthesis, and the procedure is reported so that readers can judge its coverage.

Four streams were searched. The first covered surrogate endpoint definition, validation and expedited approval, drawing on clinical epidemiology, oncology and health policy journals. The second covered pharmaceutical promotion and consumer comprehension, including direct-to-consumer advertising research and regulatory consumer studies. The third covered marketing and economics of information theory, including signalling, consumer inference, claim substantiation, disclosure and trust. The fourth covered official regulatory and institutional guidance from the United States, the European Union, the United Kingdom, Australia and the World Health Organization, used for definitions and current requirements rather than for interpretation.

Sources were included where they informed the evidentiary meaning of an endpoint, the design or effect of a pharmaceutical communication, the mechanism by which consumers form inferences, or the boundary conditions of the proposed framework. Priority went to peer-reviewed work and to primary regulatory documents. Synthesis was concept-centric. Each stream was read for what it explains, what it leaves unexplained and where its constructs could be joined, and the output is a framework with defined constructs and propositions rather than pooled evidence or a descriptive bibliography.

Table 1: Literature integration matrix

Literature stream	What it explains	What it leaves untheorised	Contribution of the present framework
Surrogate endpoint validity and expedited approval	Whether an endpoint predicts a clinical outcome, and how often surrogate-based approvals are later confirmed	How endpoint properties are transformed into lay meaning, and what that does to the market	Treats endpoint type and validation status as inputs to a communication process rather than as a purely evidentiary matter
Reporting distortion and spin in biomedical literature	How results are presented so that expert readers over-read them, and how distortion travels through press releases	Commercial message design, consumer processing and the trust consequences of over-reading	Extends the distortion chain into the commercial message and specifies the receiver-side mechanism
Pharmaceutical promotion and consumer comprehension	What advertisements contain, what audiences understand and how disclosures perform	A theoretical account of why the gap forms and what determines its size	Supplies a construct, a causal chain and testable propositions in place of descriptive findings
Information economics and signalling theory	Why quality information is asymmetric and how credible signals can be transmitted	Signals that are honest and verifiable yet still decoded as broader claims	Identifies a signalling failure driven by receiver decoding rather than by sender deception
Consumer inference and claim substantiation	How recipients fill gaps in messages, and when truthful claims mislead by implication	Evidence structures upstream of the claim, and the technical vocabulary problem specific to medicines	Anchors inference to a measurable evidentiary benchmark drawn from the trial endpoint

4. Theoretical Foundation

The framework rests on one connected explanation rather than a set of parallel theories. Information asymmetry establishes the condition. Signalling explains what firms can do about it. Consumer inference explains what recipients do with the signal. Claim substantiation supplies the normative benchmark against which the gap can be measured.

Markets in which sellers know more about quality than buyers do tend towards adverse selection unless credible quality information can be transmitted (Bikowski, 2026; Akerlof, 1970). Nelson (1970) separated goods by whether quality can be judged before purchase or only through use, and Darby and Karni (1973) added the credence category, where quality remains hard to judge even afterwards. Prescription medicines sit firmly in that category. A patient taking a therapy for a chronic condition cannot observe the counterfactual, and the clinical benefit at stake may be statistical rather than personally detectable (Stremersch and Van Dyck, 2009).

Signalling theory explains how the informed party can transmit quality information credibly (Spence, 1973). In consumer markets, signals include brand investment, warranties, third-party endorsement and the observable properties of the claim itself (Kirmani and Rao, 2000; Erdem and Swait, 1998; Connelly *et al*., 2011). In pharmaceutical communication, the endpoint wording is a signal, the presence and prominence of qualification is a signal, and the regulatory status of the product is a signal. Signalling theory is usually concerned with whether a signal is costly enough to be credible. The pharmaceutical case raises a different issue. The signal can be honest, verifiable and cheap to send, and still be decoded as something broader than it states.

That decoding is the province of consumer inference. Consumers routinely go beyond the information given, filling gaps with prior beliefs, category expectations and contextual cues (Hoch and Ha, 1986; Kardes *et al*., 2004). Inference is not a failure of attention. It is how comprehension works. Advertising research has repeatedly shown that literally true claims produce false beliefs when the omitted qualification is the part that constrains the meaning (Johar, 1995; Hastak and Mazis, 2011), and that consumers generalise from a narrow attribute claim to a broader quality judgement (Andrews *et al*., 1998). Scepticism dampens this but does not remove it, and it varies across people (Obermiller and Spangenberg, 1998; Ju, 2017).

Claim substantiation supplies the benchmark. Regulatory

regimes across jurisdictions require that a claim be supported by evidence adequate for what the claim asserts, including what it asserts by implication (FTC, 2022; TGA, 2021; MHRA, 2025). Substantiation is therefore a relation between the scope of a claim and the scope of the evidence behind it. That relational logic is what the present framework extends. Where substantiation doctrine asks whether the evidence supports the claim, the framework asks how far the evidence sits from the meaning the claim generates in the recipient, and treats that separation as a variable with consequences for inference and trust.

Trust is specified rather than assumed. Following Mayer *et al*. (1995), trust is the willingness to be vulnerable to another party based on expectations about that party's ability, benevolence and integrity. In this framework the relevant referents are the claim, the communicating firm and the regulatory system that permitted the claim, and these can move in different directions after the same disclosure.

5. Evidentiary Distance and Evidence-To-Claim Translation

Evidence-to-claim translation is the decision process through which technical trial evidence becomes a consumer-facing message. It involves selecting which endpoint to feature, choosing wording, deciding what qualification to include and how prominently, and setting the visual and emotional context.

Evidentiary distance is the separation between the clinical meaning that the featured endpoint directly supports and the patient benefit a reasonable recipient can infer from the communication built on it. Two points define the construct. It is a property of the evidence-claim pair, not of the evidence alone, so the same endpoint can produce small or large evidentiary distance depending on how it is communicated. And it is assessed against inferred meaning, not against literal wording, so a claim can be literally accurate and still sit at a large distance.

Evidentiary distance should be distinguished from three neighbours. It is not scientific uncertainty, which concerns confidence in an estimate rather than the gap between two different quantities (Han *et al*., 2011). It is not exaggeration, which is a property of the message judged against the data. And it is not deception, which is a legal and normative conclusion about whether a claim misleads a material proportion of the audience (Hastak and Mazis, 2011). A communication can carry substantial evidentiary distance while being truthful, unexaggerated and lawful. That is precisely why the construct is needed.

Claim amplification is the process by which wording, imagery, omission, prominence or context causes a bounded endpoint finding to be received as a broader treatment benefit. It is related to but distinct from spin, which describes distorted reporting of results by researchers within a scientific document (Chiu *et al*., 2017; Boutron *et al*., 2014). Claim amplification operates on the commercial side of the chain and is defined by its effect on lay recipients rather than on expert readers.

Transparency calibration is the extent to which qualifying information is prominent and comprehensible enough to keep inferred benefit within the scope the endpoint supports. It is deliberately relational. A disclosure that is technically complete but unread, or read and not understood, is poorly calibrated regardless of its accuracy. This distinguishes it from perceived brand transparency, which is a consumer judgement about a firm's general openness (Montecchi *et al*., 2024). Transparency calibration is assessed for a specific message against a specific evidentiary scope.

Consumer benefit inference is the treatment benefit a recipient believes is being offered. It is a specialisation of consumer inference (Kardes *et al*., 2004) applied to therapeutic outcome, and it can be compared with the endpoint's supported meaning to give a directional index of over-inference.

Table 2: Construct definitions, boundaries and possible operationalisation

Construct	Definition	Distinguished from	Possible operationalisation
Evidentiary distance	The separation between the clinical meaning the featured endpoint directly supports and the patient benefit a reasonable recipient can infer from the communication built on it	Scientific uncertainty, which concerns confidence in an estimate; exaggeration, judged against the data; deception, a normative and legal conclusion	Difference between an expert-rated supported-scope score and a respondent-rated inferred-benefit score on matched outcome scales
Claim amplification	The process by which wording, imagery, omission, prominence or context causes a bounded endpoint finding to be received as a broader treatment benefit	Spin, which is intra-document reporting distortion aimed at expert readers; puffery, which makes no verifiable assertion	Change in inferred benefit produced by a framing or imagery manipulation with the endpoint held constant
Transparency calibration	The extent to which qualifying information is prominent and comprehensible enough to keep inferred benefit within the scope the endpoint supports	Perceived brand transparency, which is a judgement about a firm rather than about a specific message	Composite index of disclosure prominence, unaided recall, comprehension accuracy and rated clarity
Consumer benefit inference	The treatment benefit a recipient believes is being offered after exposure to the communication	Comprehension of stated content, which measures recall rather than inferred meaning	Open-ended benefit elicitation coded against endpoint scope, plus closed items on expected survival and quality of life
Evidence-to-claim translation	The decision process through which technical trial evidence becomes a consumer-facing message	Message execution, which concerns creative delivery once the evidentiary scope is already fixed	Coded audit of endpoint selection, qualification presence and prominence across a promotional corpus

Evidentiary distance is best treated as a continuum. A claim reporting an absolute survival gain from a trial powered on survival sits at the low end. A claim reporting progression-free survival, qualified in plain language about what is not yet known about survival, sits in the middle. A claim reporting tumour shrinkage alongside imagery of an active family life, with survival unmentioned, sits at the high end. Table I sets out this gradation across endpoint types together with the corresponding safeguards.

Table 3: Endpoint types, consumer inference and evidentiary distance

Endpoint featured in the claim	What the endpoint directly supports	Plausible consumer inference	Principal source of evidentiary distance	Communication safeguard
Overall survival (reference case, not a surrogate)	Patients receiving the treatment lived longer on average than the comparator group	The treatment helps people live longer	Low. Distance arises mainly from relative rather than absolute framing	Report the absolute gain and the time frame alongside any relative figure
Progression-free survival	Time before radiographic progression or death was longer	The treatment helps people live longer and feel better	Association with survival is often weak, unquantified or absent, and quality of life is usually not established	State plainly that survival benefit is not yet known, using wording tested for comprehension
Objective response rate	A defined proportion of tumours shrank by a threshold amount	The treatment shrinks the cancer, therefore it works	Frequently single-arm with no comparator, responders are a subgroup, and no outcome link is demonstrated	Report the proportion, the absence of a comparator and what response does not establish
Laboratory or physiological markers such as HbA1c, LDL cholesterol, blood pressure or viral load	The marker moved in a favourable direction	My personal risk of the downstream event is reduced	Marker-to-outcome validity may hold for one drug class and not for another, and individual risk reduction is not the trial estimate	Separate class-level validation from product-level evidence and express benefit in absolute risk
Imaging or structural markers such as bone mineral density or plaque volume	A structural measure changed	Fewer fractures or fewer cardiac events	Structural change may not track event rates, and event outcomes are often unmeasured	Report the event outcome where measured and state clearly where it was not
Composite or scored endpoints	A combined or scored measure improved	I will feel substantially better	Statistical significance without a clinically meaningful magnitude, and composites driven by their least serious component	Report the component drivers and the minimal important difference

Note. The classification is illustrative rather than exhaustive. Evidentiary distance is a property of the evidence-claim pair, so any endpoint in this table can sit at a lower or higher position depending on how the claim is framed and qualified.

6. Conceptual Framework and Propositions

Figure 1 presents the framework. Regulatory evidence characteristics, chiefly endpoint type, degree of validation and approval pathway, set the evidentiary scope. Translation decisions determine claim framing and disclosure. Together these produce evidentiary distance, which drives claim amplification and consumer benefit inference, which in turn shape credibility and trust. Moderators operate at each stage.

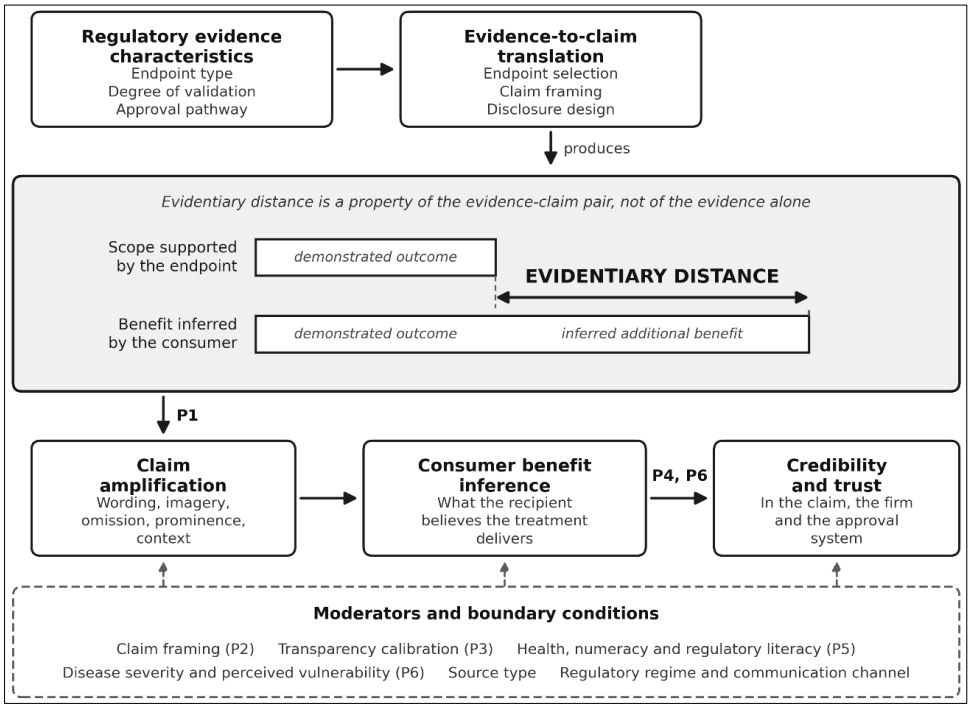

Fig 1

6.1. Evidentiary Distance and Benefit Inference

When a message reports a marker rather than an outcome, the recipient must supply the missing link. Inference research predicts that the gap will be filled with the most available and desirable interpretation, and that recipients will not spontaneously generate the qualification the communicator omitted (Hoch and Ha, 1986; Kardes *et al*., 2004). The regulatory experiments described earlier show the pattern in this exact setting (Sullivan *et al*., 2023).

P1. The greater the evidentiary distance in a pharmaceutical communication, the more likely it is that consumer benefit inference exceeds the outcome the featured endpoint supports.

6.2. Claim Framing and Amplification

Framing determines which interpretation is most accessible. Outcome-oriented language, patient imagery, testimonial and emotional context all supply a benefit schema that the endpoint itself does not carry (Applequist and Ball, 2018; Rollins *et al*., 2020). Where efficacy is stated qualitatively rather than quantitatively, the schema has still less to constrain it (O'Donoghue *et al*., 2014). Framing does not create evidentiary distance, but it converts distance into inference.

P2. Benefit-oriented claim framing strengthens the positive relationship between evidentiary distance and claim amplification, and endpoint-anchored framing weakens it.

6.3. Transparency Calibration

Qualification can close the gap, but only if it is noticed and understood. Disclosure research shows that warnings and qualifications frequently fail on prominence, comprehension or both (Stewart and Martin, 1994), while plain-language summaries of benefit and harm improve accuracy substantially (Schwartz *et al*., 2009; Schwartz and Woloshin, 2011). The regulatory experiments found that a single plain sentence about unknown survival benefit shifted expectations (Sullivan *et al*., 2023). Regulatory attention to how a qualification is presented, rather than only to whether it appears, follows the same logic (FDA, 2023).

P3. Higher transparency calibration reduces claim amplification by narrowing consumer benefit inference towards the scope the endpoint supports.

6.4. Disclosure and Credibility

Disclosing a limitation might be expected to reduce persuasion. Two-sided message research suggests the opposite can occur, because acknowledging a weakness signals candour and raises perceived trustworthiness (Eisend, 2006; Darke and Ritchie, 2007). Experimental work on communicating uncertainty in numerical and scientific claims finds that clearly expressed uncertainty has small effects on trust and does not generally undermine it (van der Bles *et al*., 2020). Applied here, an honest statement of what an endpoint does not yet show functions as a costly signal in a market where omission is the norm.

P4. Where uncertainty disclosure is comprehensible and perceived as candid, it increases source credibility relative to equally uncertain communications that omit or obscure the limitation.

6.5. Literacy as a Boundary on Correction

Disclosure works through comprehension, so its corrective effect is conditional on the recipient's capacity to process it. Health literacy and numeracy both predict how well quantitative health information is understood and used (Nutbeam, 2000; Berkman *et al*., 2011; Reyna *et al*., 2009). Regulatory literacy, meaning understanding of what approval does and does not certify, is separately limited (O'Donoghue *et al*., 2016). A disclosure that presupposes any of these can leave inflated inference intact.

P5. The corrective effect of uncertainty disclosure on consumer benefit inference is moderated by health literacy, numeracy and regulatory literacy, and is weakest where these are low.

6.6. Stakes, Reliance and Trust

In severe disease, consumers rely more heavily on credible signals precisely because they can least afford to evaluate them independently, and motivated reasoning favours optimistic readings. The same conditions raise the cost of later disconfirmation, for example when a confirmatory trial fails or an indication is withdrawn. Deception research shows that perceived misleading by a marketer generalises into distrust beyond the specific claim (Darke and Ritchie, 2007), and pharmaceutical brand credibility is itself an antecedent of consumer loyalty and advocacy (Bairrada *et al*., 2021).

P6. In high-stakes treatment contexts the effect of evidentiary distance on consumer benefit inference is stronger, and subsequent disconfirmation of the inferred benefit produces a larger reduction in trust in the claim, the firm and the approval system.

7. Regulatory and Market Boundary Conditions

The framework is not confined to direct-to-consumer prescription advertising, which is permitted in only a small number of jurisdictions. Its scope is any communication in which endpoint-derived evidence reaches a lay audience.

In the European Union, advertising prescription medicines to the general public is prohibited (European Parliament and Council of the European Union, 2001), yet disease-awareness campaigns, corporate communication, patient information and media coverage of approvals still carry endpoint-derived meaning to lay audiences, and such campaigns have been found inconsistent with promotional standards in some settings (Leonardo Alves *et al*., 2018). Where promotion to the public is permitted, the same translation decisions occur explicitly and are subject to presentation requirements (FDA, 2023). Australian and United Kingdom regimes regulate advertising of medicines to the public through codified advertising rules and substantiation obligations (TGA, 2021; MHRA, 2025), and international ethical criteria set expectations for the accuracy and completeness of promotional information (WHO, 1988).

Channel matters as much as jurisdiction. Digital and social environments have shifted a substantial share of pharmaceutical communication away from formats designed for regulatory review (Mackey *et al*., 2015), and patient influencers now operate in a space where disclosure norms and evidentiary standards are unsettled (Willis and Delbaere, 2022). Amplification in these channels is often achieved through omission and context rather than through explicit claims, which is exactly the mechanism the framework describes.

Two boundary conditions should be stated. The framework assumes a lay audience without endpoint expertise, so it does not apply to promotion directed at prescribers, where the relevant asymmetry is different (Mukherjee *et al*., 2013). And

it assumes a legally permitted communication, so it addresses lawful messages rather than off-label or fraudulent promotion.

8. Theoretical Implications

Introducing evidentiary distance changes what pharmaceutical marketing theory treats as given. Claim research has generally taken the claim as the unit of analysis and asked whether it is accurate, believable or persuasive. The framework makes the evidentiary origin of the claim a variable in its own right. Two communications with identical wording can differ in their capacity to mislead because the endpoints beneath them differ, and no message-level analysis will detect that.

For signalling theory, the case is unusual and instructive. The standard problem is separating credible from non-credible signals when senders have an incentive to imitate. Here the signal can be verifiable and honest yet still generate a receiver belief the sender never asserted. This points to a class of signalling failure driven by the receiver's decoding frame rather than by sender deception, and suggests that signal design in technical categories should be evaluated against inferred meaning rather than against sent meaning.

The framework also connects two literatures that have run in parallel. Regulatory science has documented the phenomenon in oncology without a behavioural account of it, and consumer research has developed the behavioural account without engaging clinical evidence structures. Table II sets out what each stream explains, what it leaves open and where the constructs join.

9. Managerial and Regulatory Implications

For pharmaceutical brand and communications teams, the practical shift is from asking whether a claim is defensible to asking what a claim generates. That requires pre-testing inferred benefit, not only recall and comprehension of stated content. A simple diagnostic is to ask respondents what the product does for patients and to compare the modal answer with the endpoint's supported meaning. Where the two diverge, the message carries amplification regardless of its literal accuracy.

For medical-legal-regulatory reviewers, evidentiary distance can be added as an explicit review dimension alongside substantiation. The review question becomes whether the qualification is prominent and comprehensible enough to hold inference within scope, which is a testable property rather than a matter of judgement. Table I offers a starting classification.

For agencies and copywriters, the operative discipline is to keep endpoint wording and patient-outcome wording separate, and to check whether imagery, testimonial or context is supplying an outcome claim that the copy does not make. Visual amplification is harder to detect in review than verbal amplification and deserves specific attention.

For regulators, the framework suggests evaluating disclosures by whether they correct inference rather than by whether they state facts. Evidence that a single plain sentence about unknown survival benefit changes expectations (Sullivan *et al*., 2023) indicates that well-designed qualification is achievable at low cost. It also indicates that variability in how expedited approval status is disclosed is a solvable problem (Sullivan *et al*., 2018).

For healthcare professionals and patient educators, the framework identifies where expectations are likely to have been formed before the consultation, and which endpoint types most often require correction.

10. Future Research and Measurement Agenda

The framework is designed to be tested. Evidentiary distance can be operationalised as the difference between a recipient's inferred benefit and the endpoint's supported meaning, measured on matched scales, with an expert-rated scope score used as the benchmark. Claim amplification can be measured as the increase in inferred benefit produced by a framing manipulation holding the endpoint constant. Transparency calibration can be indexed from disclosure prominence, comprehension accuracy and self-reported clarity.

Four study designs follow directly. Factorial experiments manipulating endpoint type and disclosure format would test P1 to P4, using survival and quality-of-life expectations as dependent variables. Content analyses of promotional and disease-awareness material across jurisdictions would establish the distribution of evidentiary distance in practice and extend existing endpoint-reporting audits (Wayant *et al*., 2020). Longitudinal or scenario-based designs following a confirmatory trial failure would test the trust predictions in P6, which cannot be captured in a single exposure. Cross-country designs comparing permissive and restrictive advertising regimes would test whether regulatory context substitutes for or complements message-level calibration.

Several questions sit beyond the present framework and merit separate work. Whether prescribers show the same inference pattern under time pressure is unknown. Whether repeated exposure to well-calibrated disclosure builds durable regulatory literacy, or simply produces habituation, is unresolved. And whether evidentiary distance behaves similarly for vaccines, medical devices and health-related consumer products, where the evidence structures differ, is an open empirical question.

11. Conclusion

Pharmaceutical claims can be accurate and still leave audiences believing something the evidence does not support. That outcome is not primarily a failure of honesty. It arises where a technical endpoint is translated into ordinary language for people who cannot verify the result and who have strong reasons to hope. Evidentiary distance names the separation that makes this possible and locates it where it belongs, in the relationship between the evidence and the message rather than in either one alone. The framework set out here explains how that separation is created, how framing and qualification widen or narrow it, and why the consequences run through credibility and trust rather than through comprehension alone. Surrogate endpoints are not the problem. The unexamined step between what they show and what a claim implies is.

References

1. Akerlof GA. The market for "lemons": quality uncertainty and the market mechanism. Q J Econ. 1970;84(3):488-500. doi: 10.2307/1879431.
2. Andrews JC, Netemeyer RG, Burton S. Consumer generalization of nutrient content claims in advertising. J Mark. 1998;62(4):62-75. doi: 10.1177/002224299806200405.
3. Applequist J, Ball JG. An updated analysis of direct-to-consumer television advertisements for prescription drugs. Ann Fam Med. 2018;16(3):211-6. doi:

10.1370/afm.2220.
4. Bairrada CM, Costa JF, Santos RM, Coelho A. Determinants and consequences of brand credibility: a case study in the pharmaceutical industry. Int J Pharm Healthc Mark. 2021;15(2):282-97. doi: 10.1108/IJPHM-05-2020-0037.
5. Banzi R, Gerardi C, Bertelè V, Garattini S. Conditional approval of medicines by the EMA. BMJ. 2017;357:j2062. doi: 10.1136/bmj.j2062.
6. Berkman ND, Sheridan SL, Donahue KE, Halpern DJ, Crotty K. Low health literacy and health outcomes: an updated systematic review. Ann Intern Med. 2011;155(2):97-107. doi: 10.7326/0003-4819-155-2-201107190-00005.
7. Bikowski L. Social media strategies for building trust in nonprofit hospitals: a conceptual framework. Eur J Manag Issues. 2026;34(1):21-9. https://doi.org/10.15421/192602.
8. Bikowski L. Startup ecosystems as catalysts of regional innovation and competitive advantage. Int J Innov Stud. 2026:100209. Advance online publication. https://doi.org/10.1016/j.ijis.2026.100209.
9. Biomarkers Definitions Working Group. Biomarkers and surrogate endpoints: preferred definitions and conceptual framework. Clin Pharmacol Ther. 2001;69(3):89-95. doi: 10.1067/mcp.2001.113989.
10. Boutron I, Altman DG, Hopewell S, Vera-Badillo F, Tannock I, Ravaud P. Impact of spin in the abstracts of articles reporting results of randomized controlled trials in the field of cancer: the SPIIN randomized controlled trial. J Clin Oncol. 2014;32(36):4120-6. doi: 10.1200/JCO.2014.56.7503.
11. Chiu K, Grundy Q, Bero L. "Spin" in published biomedical literature: a methodological systematic review. PLoS Biol. 2017;15(9):e2002173. doi: 10.1371/journal.pbio.2002173.
12. Ciani O, Buyse M, Drummond M, Rasi G, Saad ED, Taylor RS. Time to review the role of surrogate end points in health policy: state of the art and the way forward. Value Health. 2017;20(3):487-95. doi: 10.1016/j.jval.2016.10.011.
13. Connelly BL, Certo ST, Ireland RD, Reutzel CR. Signaling theory: a review and assessment. J Manag. 2011;37(1):39-67. doi: 10.1177/0149206310388419.
14. Darby MR, Karni E. Free competition and the optimal amount of fraud. J Law Econ. 1973;16(1):67-88. doi: 10.1086/466756.
15. Darke PR, Ritchie RJB. The defensive consumer: advertising deception, defensive processing, and distrust. J Mark Res. 2007;44(1):114-27. doi: 10.1509/jmkr.44.1.114.
16. Davis C, Naci H, Gurpinar E, Poplavska E, Pinto A, Aggarwal A. Availability of evidence of benefits on overall survival and quality of life of cancer drugs approved by European Medicines Agency: retrospective cohort study of drug approvals 2009-13. BMJ. 2017;359:j4530. doi: 10.1136/bmj.j4530.
17. Eisend M. Two-sided advertising: a meta-analysis. Int J Res Mark. 2006;23(2):187-98. doi: 10.1016/j.ijresmar.2005.11.001.
18. European Medicines Agency. Conditional marketing authorisation. Amsterdam: EMA; 2020. Available from: https://www.ema.europa.eu/en/human-regulatory-overview/marketing-authorisation/conditional-marketing-authorisation. Accessed 8 Aug 2026.
19. European Medicines Agency. Guideline on the clinical evaluation of anticancer medicinal products. Rev. 6 (EMA/CHMP/205/95 Rev.6). Amsterdam: EMA; 2024. Available from: https://www.ema.europa.eu/en/evaluation-anticancer-medicinal-products-scientific-guideline. Accessed 8 Aug 2026.
20. Erdem T, Swait J. Brand equity as a signaling phenomenon. J Consum Psychol. 1998;7(2):131-57. doi: 10.1207/s15327663jcp0702_02.
21. European Parliament and Council of the European Union. Directive 2001/83/EC of the European Parliament and of the Council of 6 November 2001 on the Community code relating to medicinal products for human use. Off J Eur Communities. 2001;L311:67. Available from: https://eur-lex.europa.eu/eli/dir/2001/83/oj/eng. Accessed 8 Aug 2026.
22. Fallowfield LJ, Catt SL, May SF, Matthews L, Shilling VM, Simcock R, *et al*. Therapeutic aims of drugs offering only progression-free survival are misunderstood by patients, and oncologists may be overly optimistic about likely benefits. Support Care Cancer. 2017;25(1):237-44. doi: 10.1007/s00520-016-3408-7.
23. US Food and Drug Administration. Clinical trial endpoints for the approval of cancer drugs and biologics: guidance for industry. Silver Spring (MD): FDA; 2018. Available from: https://www.fda.gov/regulatory-information/search-fda-guidance-documents/clinical-trial-endpoints-approval-cancer-drugs-and-biologics. Accessed 8 Aug 2026.
24. US Food and Drug Administration. Direct-to-consumer prescription drug advertisements: presentation of the major statement in a clear, conspicuous, and neutral manner in advertisements in television and radio format. Fed Regist. 2023;88:80958-84. Available from: https://www.federalregister.gov/d/2023-25428. Accessed 8 Aug 2026.
25. US Food and Drug Administration. Accelerated approval program. Silver Spring (MD): FDA; 2026. Available from: https://www.fda.gov/drugs/nda-and-bla-approvals/accelerated-approval-program. Accessed 8 Aug 2026.
26. Fleming TR. Surrogate endpoints and FDA's accelerated approval process. Health Aff (Millwood). 2005;24(1):67-78. doi: 10.1377/hlthaff.24.1.67.
27. Fleming TR, DeMets DL. Surrogate end points in clinical trials: are we being misled? Ann Intern Med. 1996;125(7):605-13. doi: 10.7326/0003-4819-125-7-199610010-00011.
28. Federal Trade Commission. Health products compliance guidance. Washington (DC): FTC; 2022. Available from: https://www.ftc.gov/business-guidance/resources/health-products-compliance-guidance. Accessed 8 Aug 2026.
29. Gyawali B, Hey SP, Kesselheim AS. Assessment of the clinical benefit of cancer drugs receiving accelerated approval. JAMA Intern Med. 2019;179(7):906-13. doi: 10.1001/jamainternmed.2019.0462.
30. Han PKJ, Klein WMP, Arora NK. Varieties of uncertainty in health care: a conceptual taxonomy. Med Decis Making. 2011;31(6):828-38. doi:

10.1177/0272989X10393976.
31. Hastak M, Mazis MB. Deception by implication: a typology of truthful but misleading advertising and labeling claims. J Public Policy Mark. 2011;30(2):157-67. doi: 10.1509/jppm.30.2.157.
32. Hoch SJ, Ha YW. Consumer learning: advertising and the ambiguity of product experience. J Consum Res. 1986;13(2):221-33. doi: 10.1086/209062.
33. Johar GV. Consumer involvement and deception from implied advertising claims. J Mark Res. 1995;32(3):267-79. doi: 10.1177/002224379503200303.
34. Ju I. The effects of advertising skepticism in consumer prescription drug advertising. Int J Pharm Healthc Mark. 2017;11(4):395-411. doi: 10.1108/IJPHM-10-2016-0054.
35. Kardes FR, Posavac SS, Cronley ML. Consumer inference: a review of processes, bases, and judgment contexts. J Consum Psychol. 2004;14(3):230-56. doi: 10.1207/s15327663jcp1403_6.
36. Kim C, Prasad V. Cancer drugs approved on the basis of a surrogate end point and subsequent overall survival: an analysis of 5 years of US Food and Drug Administration approvals. JAMA Intern Med. 2015;175(12):1992-4. doi: 10.1001/jamainternmed.2015.5868.
37. Kirmani A, Rao AR. No pain, no gain: a critical review of the literature on signaling unobservable product quality. J Mark. 2000;64(2):66-79. doi: 10.1509/jmkg.64.2.66.18000.
38. Leonardo Alves T, Poplavska E, Mezinska S, Salmane-Kulikovska I, Andersone L, Mantel-Teeuwisse AK, *et al*. Disease awareness campaigns in printed and online media in Latvia: cross-sectional study on consistency with WHO ethical criteria for medicinal drug promotion and European standards. BMC Public Health. 2018;18(1):1322. doi: 10.1186/s12889-018-6202-2.
39. MacEwan JP, Doctor J, Mulligan K, May SG, Batt K, Zacker C, *et al*. The value of progression-free survival in metastatic breast cancer: results from a survey of patients and providers. MDM Policy Pract. 2019;4(1):2381468319855386. doi: 10.1177/2381468319855386.
40. Mackey TK, Cuomo RE, Liang BA. The rise of digital direct-to-consumer advertising? Comparison of direct-to-consumer advertising expenditure trends from publicly available data sources and global policy implications. BMC Health Serv Res. 2015;15(1):236. doi: 10.1186/s12913-015-0885-1.
41. Mayer RC, Davis JH, Schoorman FD. An integrative model of organizational trust. Acad Manag Rev. 1995;20(3):709-34. doi: 10.5465/amr.1995.9508080335.
42. Medicines and Healthcare products Regulatory Agency. Blue guide: advertising and promotion of medicines in the UK. London: MHRA; 2025. Available from: https://www.gov.uk/government/publications/blue-guide-advertising-and-promoting-medicines. Accessed 8 Aug 2026.
43. Mintzes B. Advertising of prescription-only medicines to the public: does evidence of benefit counterbalance harm? Annu Rev Public Health. 2012;33(1):259-77. doi: 10.1146/annurev-publhealth-031811-124540.
44. Montecchi M, Plangger K, West DC, de Ruyter K. Perceived brand transparency: a conceptualization and measurement scale. Psychol Mark. 2024;41(10):2274-97. doi: 10.1002/mar.22048.
45. Mukherjee A, Limbu Y, Wanasika I. A review of research on direct-to-consumer advertising of prescription drugs. Int J Pharm Healthc Mark. 2013;7(3):226-43. doi: 10.1108/IJPHM-07-2013-0037.
46. Naci H, Smalley KR, Kesselheim AS. Characteristics of preapproval and postapproval studies for drugs granted accelerated approval by the US Food and Drug Administration. JAMA. 2017;318(7):626-36. doi: 10.1001/jama.2017.9415.
47. Nelson P. Information and consumer behavior. J Polit Econ. 1970;78(2):311-29. doi: 10.1086/259630.
48. Nutbeam D. Health literacy as a public health goal: a challenge for contemporary health education and communication strategies into the 21st century. Health Promot Int. 2000;15(3):259-67. doi: 10.1093/heapro/15.3.259.
49. Obermiller C, Spangenberg ER. Development of a scale to measure consumer skepticism toward advertising. J Consum Psychol. 1998;7(2):159-86. doi: 10.1207/s15327663jcp0702_03.
50. O'Donoghue AC, Sullivan HW, Aikin KJ, Chowdhury D, Moultrie RR, Rupert DJ. Presenting efficacy information in direct-to-consumer prescription drug advertisements. Patient Educ Couns. 2014;95(2):271-80. doi: 10.1016/j.pec.2013.12.010.
51. O'Donoghue AC, Sullivan HW, Williams PA, Squire C, Betts KR, Fitts Willoughby J, *et al*. Consumers' understanding of FDA approval requirements and composite scores in direct-to-consumer prescription drug print ads. J Health Commun. 2016;21(8):927-34. doi: 10.1080/10810730.2016.1179367.
52. Prasad V, Kim C, Burotto M, Vandross A. The strength of association between surrogate end points and survival in oncology: a systematic review of trial-level meta-analyses. JAMA Intern Med. 2015;175(8):1389-98. doi: 10.1001/jamainternmed.2015.2829.
53. Prentice RL. Surrogate endpoints in clinical trials: definition and operational criteria. Stat Med. 1989;8(4):431-40. doi: 10.1002/sim.4780080407.
54. Reyna VF, Nelson WL, Han PK, Dieckmann NF. How numeracy influences risk comprehension and medical decision making. Psychol Bull. 2009;135(6):943-73. doi: 10.1037/a0017327.
55. Rollins B, Huh J, Bhutada N, Perri M. Effects of endorser type and testimonials in direct-to-consumer prescription drug advertising (DTCA). Int J Pharm Healthc Mark. 2020;15(1):1-17. doi: 10.1108/IJPHM-06-2019-0042.
56. Schwartz LM, Woloshin S. Communicating uncertainties about prescription drugs to the public: a national randomized trial. Arch Intern Med. 2011;171(16):1463-8. doi: 10.1001/archinternmed.2011.396.
57. Schwartz LM, Woloshin S, Welch HG. Using a drug facts box to communicate drug benefits and harms: two randomized trials. Ann Intern Med. 2009;150(8):516-27. doi: 10.7326/0003-4819-150-8-200904210-00106.
58. Spence M. Job market signaling. Q J Econ. 1973;87(3):355-74. doi: 10.2307/1882010.
59. Stewart DW, Martin IM. Intended and unintended consequences of warning messages: a review and synthesis of empirical research. J Public Policy Mark. 1994;13(1):1-19. doi: 10.1177/074391569401300101.

60. Stremersch S, Van Dyck W. Marketing of the life sciences: a new framework and research agenda for a nascent field. J Mark. 2009;73(4):4-30. doi: 10.1509/jmkg.73.4.004.
61. Sullivan HW, O'Donoghue AC, David KT, Patel NJ. Disclosing accelerated approval on direct-to-consumer prescription drug websites. Pharmacoepidemiol Drug Saf. 2018;27(11):1277-80. doi: 10.1002/pds.4664.
62. Sullivan HW, O'Donoghue AC, Ferriola-Bruckenstein K, Tzeng JP, Boudewyns V. Patients' understanding of oncology clinical endpoints: environmental scan and focus groups. Oncologist. 2020;25(12):1060-6. doi: 10.1634/theoncologist.2020-0402.
63. Sullivan HW, O'Donoghue AC, Boudewyns V, Paquin RS, Ferriola-Bruckenstein K. Patient understanding of oncology clinical trial endpoints in direct-to-consumer television advertising. Oncologist. 2023;28(7):e542-53. doi: 10.1093/oncolo/oyad064.
64. Therapeutic Goods Administration. Therapeutic Goods (Therapeutic Goods Advertising Code) Instrument 2021. Canberra: TGA; 2021. Available from: https://www.legislation.gov.au/F2021L01661/latest. Accessed 8 Aug 2026.
65. van der Bles AM, van der Linden S, Freeman ALJ, Spiegelhalter DJ. The effects of communicating uncertainty on public trust in facts and numbers. Proc Natl Acad Sci U S A. 2020;117(14):7672-83. doi: 10.1073/pnas.1913678117.
66. Vokinger KN, Kesselheim AS, Glaus CEG, Hwang TJ. Therapeutic value of drugs granted accelerated approval or conditional marketing authorization in the US and Europe from 2007 to 2021. JAMA Health Forum. 2022;3(8):e222685. doi: 10.1001/jamahealthforum.2022.2685.
67. Wayant C, Aran G, Johnson BS, Vassar M. Evaluation of selective outcome reporting bias in efficacy endpoints in print and television advertisements for oncology drugs. J Gen Intern Med. 2020;35(10):2853-7. doi: 10.1007/s11606-020-06028-1.
68. World Health Organization. Ethical criteria for medicinal drug promotion. Geneva: WHO; 1988. Available from: https://iris.who.int/handle/10665/38125. Accessed 8 Aug 2026.
69. Willis E, Delbaere M. Patient influencers: the next frontier in direct-to-consumer pharmaceutical marketing. J Med Internet Res. 2022;24(3):e29422. doi: 10.2196/29422.
70. Woloshin S, Schwartz LM, Tremmel J, Welch HG. Direct-to-consumer advertisements for prescription drugs: what are Americans being sold? Lancet. 2001;358(9288):1141-6. doi: 10.1016/S0140-6736(01)06254-7.
71. Yavchitz A, Boutron I, Bafeta A, Marroun I, Charles P, Mantz J, *et al*. Misrepresentation of randomized controlled trials in press releases and news coverage: a cohort study. PLoS Med. 2012;9(9):e1001308. doi: 10.1371/journal.pmed.1001308.