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Sabine Weckbach *Editor*

Incidental Radiological Findings

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Springer

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ISSN 0942-5373 ISSN 2197-4187 (electronic)
Medical Radiology
ISBN 978-3-319-42579-5 ISBN 978-3-319-42581-8 (eBook)
DOI 10.1007/978-3-319-42581-8

Library of Congress Control Number: 2017937774

Printed on acid-free paper

This Springer imprint is published by Springer Nature
The registered company is Springer International Publishing AG
The registered company address is: Gewerbestrasse 11, 6330 Cham, Switzerland

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Part I

Introduction

Incidental Findings: Definition of the Concept

Reinold Schmücker

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Abstract

In a broad sense, any findings can be called incidental that occur in the context of medical diagnostics and that potentially affect the health (including the reproductive capacities) of a living being – if the diagnostic means were not intended to produce such findings. It would be wrong to only talk about an incidental finding once the relevance for the health or reproductive capacity of the concerned individual has been established. The concept of an incidental finding rather includes – in its broad as well as narrow sense, which will be explained in the next paragraph – both marginal findings with no clinical relevance and false positive findings. This use of the concept makes sense, because the artefactual character of false positive findings in particular usually only becomes clear after further evaluation. Since this evaluation would not take place without the misleading primary finding, the concept of a finding cannot plausibly depend on the factual correctness or clinical relevance of diagnostic discoveries.

This chapter is derived from my handbook entry Schmücker (2013).

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Med Radiol Diagn Imaging (2016)
DOI 10.1007/174_2016_96, © Springer International Publishing Switzerland
Published Online: 17 Dec 2016

1 Incidental Findings in a Broad Sense

In a broad sense, any findings can be called incidental that occur in the context of medical diagnostics and that potentially affect the health (including the reproductive capacities) of a living being – if the diagnostic means were not intended to produce such findings. It would be wrong to only talk about an incidental finding once the relevance for the health or reproductive capacity of the concerned individual has been established. The concept of an incidental finding rather includes – in its broad as well as narrow sense, which will be explained in the next paragraph – both marginal findings with no clinical relevance and false positive findings. This use of the concept makes sense, because the artefactual character of false positive findings in particular usually only becomes clear after further evaluation. Since this evaluation would not take place without the misleading primary finding, the concept of a finding cannot plausibly depend on the factual correctness or clinical relevance of diagnostic discoveries.

Incidental findings understood in this sense can occur in the context of research in life sciences or while diagnostic means are employed to confirm the presence of a certain disease. They can also occur when magnetic resonance images are taken for an anatomical atlas or when a follow-up examination for a cured disease shows indications of a different disease.

Diagnostic findings that occur in the context of the doctor-patient relationship while searching for the cause of certain symptoms, but that do not comply with the doctor's expectations concerning this cause, are not incidental findings – not even according to the broad concept of incidental findings. The examination is aimed at establishing findings that would explain the reported symptoms, even if those findings do not comply with the physician's expectations. Diagnostic findings that occur in the context of *direct-to-consumer* genetic analyses or *direct-to-consumer* whole-body MRI examinations that are offered by commercial companies as individual check-ups also do not count as incidental findings. For there is, although no treatment contract is involved here, a contractual relationship between the subject of the preventive examination and the provider of the latter that resembles the relationship between doctor and patient in at least one respect, due to the preventive aim it is based on: the purpose of the contract and the examination is to collect information relevant for the subject's health. This information can help the subject make an informed decision about measures that will serve sustain her health for as long as possible. Even in the broad sense of the concept, it is *not* an instance of incidental findings if (a) a diagnosis is carried out, because the examined person demanded it – even without presenting any symptoms – in order to find out about a potential need for medical intervention or (b) a cause of the patient's symptoms is found that differs from what is expected by the physician who is responsible for the diagnosis. In the latter case, the findings differ from what is expected or considered likely by the physician. So the findings are unexpected, but not incidental. It is not the case that the use of the diagnostic means did not intend to produce the findings. This becomes clear once we consider the intention of the physician when employing diagnostic means. The physician does not primarily examine the patient with the aim of finding the cause of a symptom or confirming the presence of a certain disease. She rather wants to find out which therapeutic measures should be undertaken for the patient's benefit. The physician's intention is not primarily to confirm her own suspicion concerning the cause of the symptoms. The aim is usually rather to cure the patient as soon as possible. This can also be seen in the fact that an experienced physician will abstain from any further diagnostic procedures if she is confident that further differential diagnostics will be irrelevant for the indication of adequate therapeutic measures. In this case, any further examination would be unnecessary for the treatment of the patient and would only be carried out for the sake of confirming the physician's hypothesis. Since the latter is not the aim of the physician's conduct, no further examinations are required.

The occurrence of an incidental finding can nowadays not be regarded as unexpected. It has

become evident – and is a matter of basic knowledge in modern research – that the use of high-resolution imaging diagnoses in medical studies yields a relatively high number of findings that the study was not aimed at detecting (Rangel 2010, 124). In brain MRI scans, 1–8% of subjects featured incidental findings that were considered in need of further examination (Katzman et al. 1999; Alphs et al. 2006; Weber and Knopf 2006; Vernooij et al. 2007; Schleim et al. 2007; Gupta and Belay 2008). In cohort studies employing whole-body MRI, the number of incidental findings is even higher (Langanke and Erdmann 2011, 206). Unexpected findings neither are always incidental nor are incidentally discovered findings always unexpected. Therefore it would be inadequate to characterize incidental findings as unexpected findings (pace, e.g. Illes et al. 2006, 783; Heinemann et al. 2007, A1982). Incidental findings should rather be characterized as unintended findings whose discovery was not intended by a treating physician or medical researcher. Their discovery was not intended, because the intention of a treating physician is not – in contrast to, e.g. the provider of direct-to-consumer whole-body MRI examinations – to discover a clinically not (yet) manifested disease, and the intention of the researcher in life sciences is not to provide a diagnosis for the subject's disease.

2 Incidental Findings in a Narrow Sense

In the relevant literature, the concept of incidental findings is, however, often used in a different, narrower, sense than the one described above. According to this narrow understanding, incidental findings are characterized by three features:

1. They occur in participants during a scientific study.
2. They potentially affect the health or reproductive capacities of the concerned participant.
3. They are findings, the discovery of which was not intended in the context of the study's aim.

Incidental findings in this narrower sense – based on a suggestion by Wolf et al. (2008: 219) – are only those unintended findings that occur in the context of scientific research. Incidental findings in this narrow sense raise ethical problems. These problems are not raised by the broad sense according to which such findings can also occur in the context of the doctor-patient relationship. If there is a doctor-patient relationship, it is clear that strategies for avoiding the discovery of any incidental findings are illegitimate. The aim of gaining information about therapeutic measures that should be taken for the patient's benefit does not allow for avoiding certain findings. The existence of a doctor-patient relationship also means that the non-disclosure of an incidental finding cannot be justified but for it is in the immediate interest of the patient. If there is no doctor-patient relationship, however, avoiding findings and non-disclosure may not always be illegitimate.

3 Incidental Finding or Signal Abnormality?

Independently of the diagnostic methods that are employed, specific data can only be called incidental findings if they are registered as a deviation from the norm, an abnormality and hence a potential symptom. Incidental findings do not occur independently of their interpretation as *potential* symptoms. They are always the result of an at least rudimentary assessment, because they are categorized based on the comparison with an expectation that is derived from other data, or with the norm.

Heinemann et al. (2009: 2–3) distinguish between a "signal abnormality […] in the collected image data that is detected by the researcher while inspecting and analysing the data with respect to their usability for the collective scientific evaluation of the research study" and a "signal abnormality with respect to a potential clinical relevance for the individual study participant." This distinction is, however, artificial. It presupposes that it is, in principle, possible for the researcher to observe a signal abnormality as such without, at the same time, seeing it as a potential indication of a disease. Even if this is theoretically conceivable, it is practically impossible for a trained doctor or a

similarly competent researcher. A researcher could deliberately *ignore* the indicative character of an abnormality and the clinical relevance for the participant. She cannot, however, evaluate (imaging) data without referring to her specific knowledge about the subject nor can she only refer to that knowledge to the extent required for the aim of the study *without intending such a limitation of the use of her knowledge*. Brain researchers cannot, as Schleim et al. (2007: 1044) concede, "take their entire measurements with closed eyes." The possibility of incidental findings therefore raises an important normative question: is it legitimate to evaluate the data collected in research with human subjects by only partially making use of the available knowledge about the analysis of data? The question is, in particular, whether it is legitimate to abstain from the use of such knowledge in research with human subjects, if using that knowledge could lead to a discovery that is potentially clinically relevant for the subject. This normative question requires a convincing normative answer. It should not be covered up by conceptual distinctions suggesting that discovering abnormalities in study participants could not only be separated from discovering potential disease symptoms analytically but also in research practice.

4 The Differing Indicative Dignity of Incidental Findings

Incidental findings do not always have the same indicative dignity. Three different classes of dignity can be distinguished from each other here. The first class contains those incidental findings whose clinical relevance is evident. These could be abnormalities or changes that evidently indicate, for example, a renal tumour. The second class contains incidental findings that – according to the current state of medical knowledge – are not clinically significant. One example would be an arachnoid cyst found during a brain MRI examination. The third class contains abnormalities whose clinical relevance is unclear, such as an intervertebral disc degeneration that is only clinically relevant if the anamnesis or examination of the person concerned yields indications of complaints or failure of the nerves. Findings of this type are more common in research contexts than in clinical contexts, because in research, a very high number of subjects is examined – and not only in one but in many respects. For this class, it might be thought maintainable to merely speak of signal abnormalities, because there is no (sufficient) evidence that the abnormality is indicating a disease. However, assigning an abnormality to this class always presupposes an evaluation by the researcher and thus her use of her knowledge about analysing the relevant data. Therefore the possibility of abnormalities belonging to this class does not contradict the above statement that the evaluator's knowledge about analysing the relevant data always influences the evaluation of the participants' data. This suggests that abnormalities of this class should also be characterized as incidental findings, if necessary.

Further distinctions can be made within the three classes of dignity. In particular, it would be appropriate to differentiate between clinically relevant incidental findings where a medical intervention is required and those where a risk assessment suggests the contrary. For these distinctions, knowledge about the natural history of the disease in question is required, and for many incidental findings, this is still missing.

5 The Context of the Occurrence of Incidental Findings

Incidental findings (in the narrow sense) concern diseases for which the participant showed no symptoms prior to the study. Findings of this kind occur in different research contexts. Currently they mostly occur (a) in the context of clinical studies with the aim of reviewing the therapeutic efficacy of a drug or a certain medical intervention and of reviewing their potential adverse effects in order to judge whether the latter are acceptable; (b) in the context of fundamental research in life sciences with the aim of deepening the scientific understanding of human beings or the interaction between human beings and their environment by examining, e.g. the function of certain brain regions or the reactions of the brain to specific external stimuli; (c) in medical fundamental research with the aim of benefitting

the health care of future patient generations. The currently most prominent field of fundamental research in life sciences, where a large number of incidental findings occur, is the neuroscientific localization of specific functions in the human brain. In medical fundamental research, a large number of incidental findings occur in epidemiological cohort studies, which include MRI scans in most cases. Clinical studies include medical interventions; fundamental research does not (besides interventions that are necessary for a diagnosis such as the infusion of a contrast medium, the application of stimuli and the like). These three types of research contexts also differ from each other in their respective type of study participant. Clinical studies are mostly carried out with "patient subjects" (Heinemann et al. 2009: 3), i.e. with participants who already show a clinically manifest disease and hope for a (higher) chance of a cure by participating in the study. Neuroscientific fundamental research is often carried out with young, healthy subjects, where the chances of a disease-related partial dysfunction of the brain are relatively low. Neuroscientific studies also include patients who had a stroke, however, in order to investigate neuroplasticity. Population-based epidemiological studies require representative random samples from the general public.

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