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FAST EFFECTIVE READING TRAINING

Supplementary Comprehension Exercise

"Trials and Tribulations in Medicine"

Instructions for doing this exercise:

1. *It is best to print all pages before you read but this exercise can be undertaken on a screen.*
2. *Just before you start to read the text, start stopwatch on your phone / computer or note time on a watch.*
3. *When finished, check your time and convert to reading speed from the chart. Record speed in the results box at the end of the text.*
4. *There are ten multiple-choice questions at the end, do these if you want to check your % comprehension. Get 6 answers right and you have 60% comprehension, 7 right and it is 70% comprehension. There is only ever one true answer to a question and there are no trick questions.*
5. *Check your answers against those supplied on separate attachment. Add your % score to the results box.*

Trials and Tribulations in Medicine

When investigators undertake clinical trials on behalf of the pharmaceutical industry, there is often a lack of appreciation of the common and the different aims of these two groups. This results in failure to achieve a satisfactory outcome for either group. This article explores the relationship between the investigator and the pharmaceutical industry, and suggests how a mutual understanding of both the differences and similarities between them will improve the standard of clinical trials.

Clinical trials are crucial in determining the clinical utility of a drug, although their importance in influencing prescribing is controversial. A combination of increasing regulatory requirements and a lack of precision in the assessment of new drugs, especially anti-bacterials, has led to a mushrooming of clinical trials. Doctors are overloaded with clinical trial results, without a clear understanding of the validity of them, and have been unable to accept the pronouncements of the university experts on clinical trials.

Moreover, the results of many clinical trials with antibiotics could be predicted just from sensitivity tests of recent isolates from the trial centre. The author of a recent paper considered that there is no point in continuing to produce new drugs if it is impossible to evaluate them. He suggested that more emphasis should be placed on statistical design of clinical trials, especially to avoid Type II error (finding no difference between treatments when they do differ), and on comparative in-vitro tests, diagnostic methods and measurement of response.

Clinical trials are commissioned by the pharmaceutical industry to evaluate, register and market new products. Pharmaceutical companies are interested in both safety and efficacy. Over the last 15 years increasing emphasis has been on safety. Recently, drug regulatory bodies have been asking for an estimate of the benefit-to-risk ratio of the product, a development which is reflected in the new requirements for a critical expert report signed by appointed experts. Many regulatory authorities make an estimation (some covertly) of the need for a particular product in relation to medicines that are already available.

Against this background, information on differences between products is required earlier in a drug's development, to obtain early registration and to promote new products successfully. It follows therefore that there is a need to perform large-scale multi-investigator or multi-centre controlled trials with high statistical power early in the development life of a drug. Basic standards for the conduct of clinical trials have been set up through drug regulatory agencies such as the F.D.A., through their guidelines on good clinical practice, and have generally been accepted by the pharmaceutical industry. The Association of the Pharmaceutical Industry has published a report on 'Good Clinical Practice' for the guidance of member companies.

Pharmaceutical physicians bridge the gap between investigators and the pharmaceutical industry. Most medical advisers in the industry consider pharmaceutical medicine as a

speciality in its own right. With increasing regulation, the correspondingly growing burden of obtaining and processing data falls on them. The biggest demand on their time is the preparation of regulatory documents such as clinical trial reports and overviews. With the Committee on Safety of Medicines' increasingly stringent registration process, this usually takes 6-12 months at the end of a 3-5 year clinical programme.

Supplementary information is usually required. It is possible that medical advisers may be employed almost fully on regulatory issues for two or more years at a time. However, amidst all this, prescribing doctors should note that the medical adviser is a potent and valuable source of information about the product.

The role of the Clinical Research Associate, who is usually a scientifically qualified graduate, is now well established. Much of the role involves the planning and monitoring of clinical studies to ensure that accepted standards are achieved, overseeing logistical aspects such as drug supply, checking data and presentation of results in reports to regulatory bodies. Without the expertise of the pharmaceutical physician or clinical research associate clinical trials would be poorer. The pharmaceutical industry is criticised for producing poor clinical trials but pharmaceutical companies do not perform clinical trials alone. The blame should be shared by the doctor who performs the clinical trials on behalf of the company.

Study of the effects of anti-infective often gives valuable, more general, information about the disease processes and their management. Scientific status and interest are important motivating factors in setting up clinical trials. The pharmaceutical industry is pleased to increase knowledge in disease areas provided that useful data are also generated about their drug. A good example of this is the development of improved sepsis scoring systems in industry-sponsored antibiotic clinical studies. This sepsis scoring should allow for more reliable analysis of multi centre trials as well as increasing knowledge of infectious processes.

Doctors should have a more critical approach to the interpretation of clinical trials. Overall efficacy results from uncontrolled trials are meaningless. A 100% cure in fit patients with mild infections may be worse than a 70% cure in similar infections caused by the same pathogen. Similarly a 100% disappearance of bacteria from blood cultures under the influence of antibiotics is the norm and does not necessarily mean that all septicaemic patients will respond.

However, well performed non-comparative studies done early in the evaluation of an antibiotic render valuable information on the antibiotics' clinical utility and should not be dismissed. Indeed, more is usually learned from the failures than the successes.

Now check your time, convert it into reading speed from the chart on the following page, and record it in the left-hand portion of the results box below.

Speed in wpm	**% comp.**

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Time/Speed Conversion Chart

"Trials and Tribulations in Medicine"

Minutes

Seconds	0	1	2	3	4	5	6	7	8	9
0	---	890	445	297	221	179	152	130	114	100
5	---	840	437	291	222	177	150	129	113	101
10	4950	780	420	287	218	174	148	127	112	100
15	3300	725	404	280	213	173	146	126	111	99
20	2475	680	390	273	210	171	144	124	110	98
25	1980	642	377	266	204	167	142	123	109	97
30	1613	607	364	260	202	165	140	122	108	96
35	1400	574	352	254	198	162	139	120	107	95
40	1240	546	342	248	195	160	137	119	106	94
45	1100	520	331	243	191	158	135	118	105	93
50	990	496	321	237	188	156	133	116	104	92
55	940	475	312	232	185	154	131	115	103	91

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Questions - Trials and Tribulations in Medicine

Circle your answers

1. **Which of the following is *not* a reason for a pharmaceutical company to commission a clinical trial?**

   a. Register a new drug
   b. Develop a new drug
   c. Market a new drug
   d. Evaluate a new drug

2. **According to the author, what has become the biggest burden for pharmaceutical physicians?**

   a. Preparing regulatory documents
   b. Ensuring laboratory safety
   c. Finding voluntary test subjects
   d. Hiring qualified employees

3. **Which of the following was *not* a recommendation for improving clinical trials?**

   a. More emphasis on the trial's statistical design
   b. Careful screening of laboratory technicians
   c. Adding comparative in-vitro tests
   d. Improving diagnostic methods

4. **Which of the following was listed as a responsibility of the Clinical Research Associate?**

   a. Managing the budget used to fund the clinical trials
   b. Addressing the concerns of the volunteer test subjects
   c. Planning and monitoring of clinical studies
   d. Ensuring accuracy of the reported data

5. **According to the author, which of the following has contributed to the dramatic increase in clinical trials?**

   a. Rise in lawsuits from users of prescription drugs
   b. Lack of precision in new drug assessment
   c. Lack of qualified staff in the pharmaceutical industry
   d. Decrease in funding provided by government

6. **Since regulatory bodies are now requesting an estimate of a drug's benefit-to-risk ratio, what new requirement has been added to clinical trials?**

   a. A senior staff scientist must provide weekly reports to the regulatory body.
   b. The pharmaceutical company must hire more accountants to handle the work.
   c. A critical expert must "sign-off" on the clinical trial.
   d. The laboratory must provide proof of insurance to cover potential lawsuits.

7. **Who establishes the standards for the conduct of clinical trials?**

   a. A pharmaceutical industry standards committee
   b. The lead physician conducting the trial
   c. A panel of experts appointed by the clinical trial laboratory
   d. None of the above

8. **What advice does the author give to doctors who rely on the results of clinical trials?**

   a. They should foster a close relationship with the pharmaceutical physicians.
   b. The opinions of university experts should carry the most weight.
   c. They should compare the results to tests within the same class of drugs
   d. Doctors should adopt a more critical approach to their interpretation.

9. **Since many regulatory agencies want to compare a trial drug with those already available, what major change does the author recommend for clinical trials?**

   a. Increase lobbying efforts of the regulatory agency.
   b. Conduct the trials at multiple testing centres.
   c. Conduct more thorough market research before committing to a clinical trial.
   d. Re-examine the pharmaceutical company's testing practices.

10. **What is the main purpose of a clinical trial?**

    a. To determine the usefulness of a drug
    b. To encourage investment in a pharmaceutical company
    c. To compare a new drug against others already on the market
    d. None of the above

Now check your answers against the correct ones on the "answers" page and enter the % in the results box alongside your reading speed.